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THE RELATIONSHIP BETWEEN BIOPHOTOMETER TESTS AND THE VITAMIN A CONTENT OF THE BLOOD OF CHILDREN

WILLIAM S. BAUM, M.D., AND AUGUSTA B. MCCOORD, PH.D.
ROCHESTER, N. Y.

INTRODUCTION

THE relationship between vitamin A deficiency and nutritional night blindness is now well established.[1] Clinical observations have shown conclusively that nutritional night blindness in man can be cured by vitamin A. It is also possible to produce night blindness in animals by diets deficient in vitamin A, and the condition so produced is curable by the vitamin. Parinaud[2] first suggested that visual adaptation to dim light depends upon the presence of visual purple in the rods of the retina. Various investigators have shown the relationship between speed and amount of re-formation of visual purple in the retina and the presence of ample vitamin A. Fridericia and Holm,[3] by direct examination of the retina, showed that, in rats fed on a vitamin A-deficient diet, visual purple re-formed more slowly than it did in rats fed on a normal diet. Holm[4] demonstrated that rats fed on a vitamin A-deficient diet showed evidence of night blindness. Wald[5] proved that visual purple is a complex substance which contains vitamin A and that the formation of visual purple, both in rate and amount, depends upon the presence of adequate vitamin A.

Guilbert and Hart[6] found night blindness to be the first detectable clinical symptom of vitamin A deficiency in cattle. The minimum carotene requirement for several species of animals studied was ascertained to be from 25 to 30 micrograms per kilogram of body weight daily. Guilbert, Miller, and Hughes[7] observed that, in animals suffering from night blindness, the stores of vitamin A in the liver were practically exhausted. Moore[8] found that calves fed low carotene rations developed nyctalopia, papillary edema, and a permanent type of blindness associated with constriction of the optic nerve. These conditions were prevented by the addition of crystalline carotene to the low carotene diet.

From the Department of Pediatrics, University of Rochester School of Medicine and Dentistry.

Many clinical investigations have been performed on visual adaptation in dim light to detect vitamin A deficiency of a mild degree. Using the Birch-Hirshfeld photometer, Jeans and Zentmire[9] reported that 45 children in a group of 213 had subnormal dark adaptation. Further observation on twenty-one subjects of the subnormal group showed a return to normal adaptation in an average period of twelve days on a "good" diet including cod-liver oil. Snelling,[10] using the same instrument and similar technique, detected 63 subjects with poor adaptation in a group of 163. Improved dark adaptation on cod-liver oil therapy was noted in this series.

Jeans and Zentmire,[11] conducting a survey of Iowa school children with the same instrument, found evidence of subnormal dark adaptation in more than 26 per cent of rural, village, and urban children. A larger percentage of cases showing subnormal dark adaptation was found in those children belonging to the lower economic level. All but three of seventy-eight patients classed as definitely deficient regained normal dark adaptation under cod-liver oil therapy.

Jeghers,[12] testing a series of adults with the same instrument, found some correlation between poor dark adaptation and subjective evidence of night blindness. He later found evidence of varying degrees of abnormal dark adaptation in from 35 to 67 per cent of his subjects. A majority of the subjects improved under cod-liver oil therapy. Park,[13] using this instrument, was impressed by finding poor dark adaptation in patients who furnished suggestive clinical evidence of vitamin A deficiency. Maitra and Harris[14] tested a series of 200 school children in England with a similar instrument and found that from 22 to 36 per cent of the group exhibited poor dark adaptation. Almost all of the subnormal cases returned to normal under vitamin A therapy.

On the other hand, Snelling,[15] in a second study of sixty-four patients, using the same instrument as he had previously, noted marked variation on repeated readings with the same children and observed no consistent difference before and after cod-liver oil therapy. This observer concluded that the photometer was unsatisfactory for the estimation of small variations in dark adaptation.

Jeans, Blanchard, and Zentmire[16] introduced the biophotometer of the Frober-Faybor Company, especially devised for the dark adaptation test and constructed to overcome some of the difficulties of the Birch-Hirshfeld photometer and to furnish greater ease and speed of operation. The instrument and suggested technique for use are fully described in Jean's report,[16] together with data on children tested.

Jeghers,[12] testing 163 medical students with the biophotometer, found 35 per cent with poor dark adaptation; of these cases, 12 per cent showed some clinical manifestation of deficiency. There was good correlation between history of inadequate diet and poor adaptation. Corlette and co-workers,[17] in a group of fifty adult patients from their clinic, found twenty-two with low original readings; all but one of these subjects showed definite improvement after from four to six weeks of vitamin A therapy. Schuck and Miller[18] tested ninety-four subjects with the biophotometer; those with poor dark adaptation were retested, and sixteen subjects were found who exhibited poor dark adaptation when the readings were repeated. One-half of the subnormal group was treated with vitamin A therapy, and one-half was used as a control. Weekly readings revealed that the subjects receiving vitamin A showed improved adaptation, whereas the control group did not.

Gridgeman and Wilkinson[19] used a different technique in testing 102 subjects with the biophotometer. These investigators used as their criterion of dark adaptation the number of seconds necessary after bleaching for the subject to discern the center dot of the quincunx, which was kept constantly illuminated.

With this technique, 32 per cent of the group were found to be subnormal; of the subnormal group, those treated with vitamin A showed improved dark adaptation, whereas the control group failed to improve.

In the hands of other investigators, however, the results obtained by the biophotometer have been subjected to criticism. Palmer and Blumberg,[20] testing a series of patients with this instrument, noted marked variability in the results of successive tests and that improvement occurred with repetition of the test, whether or not the child received vitamin A. They believed this improvement was due to a learning factor. Palmer and Blumberg concluded that this method of detecting mild vitamin A deficiency was neither reliable nor accurate.

Isaacs, Jung, and Ivy,[21] examining a group of students, failed to find correlation between biophotometer readings, vitamin A intake, and clinical signs and symptoms of vitamin A deficiency. These workers pointed out very clearly what they called the "centripetal drift," i.e., if the observed readings in a group are distributed by chance (and do not depend upon a low intake of vitamin A), and if one re-examines only the persons who had low readings, then the average second reading will be higher in the group originally low. It is, therefore, necessary to re-examine the originally high group.

Snelling,[22] testing a series of patients with the biophotometer before and after vitamin A therapy, failed to find the expected correlation in readings. This observer concluded that the biophotometer was not satisfactory for detecting such variations in dark adaptation as might be produced by vitamin A deficiency. Furthermore, Booher and Williams[23] had their biophotometer calibrated by the Bureau of Standards and found that the illumination values did not agree with the millifoot candle (m.f.c.) readings of the instrument. Of 106 subjects tested, six of the poorest group and seven of the intermediate group were given vitamin A therapy for four weeks and then retested. Eight subjects showed no improvement, and five improved. Repeated readings on the same subjects showed no evidence of a learning factor. These workers concluded that, if the biophotometer were equipped with means of frequent calibration of light intensities, it might be adequate for detecting mild disadaptation.

Wald, Jeghers, and Arminio,[24] using an instrument with which both rod and cone adaptation could be measured, found that a subject maintained on a vitamin A-deficient diet showed poor dark adaptation and that improvement followed the addition of vitamin A to the diet; the addition of carotene instead of vitamin A resulted in much more rapid improvement. These investigators noted that in dark adaptation the behavior of the rods and cones is closely parallel. Hecht and Mandelbaum,[25] using the Hecht-Shaler adaptometer, tested a group of 110 subjects; the data considered to be of quantitative value were the final cone threshold, the final rod threshold, and the cone-rod transition time. Eleven of this group fell in the extreme upper threshold range; these subjects showed no evidence of vitamin A deficiency, and five out of six of these subjects showed no change on a high vitamin A diet continued for from four to five weeks. Four subjects, maintained on a vitamin A-deficient diet, showed increased threshold reading for both rods and cones, with slow improvement noted when vitamin A therapy was instituted. Dietary avitaminosis did not affect the cone-rod transition time. Haig, Hecht, and Patek[26] noted that, in subjects with avitaminosis due to cirrhosis of the liver, the cone-rod transition time was increased. Kimble and Gordon,[27] using the biophotometer, noted that subjects with poor dark adaptation and low blood vitamin, who failed to improve on a course of vitamin A therapy, showed a rapid return to normal of both the biophotometer reading and the blood vitamin when riboflavin was added to the diet. In some cases where riboflavin failed to produce this result, ascorbic acid caused satisfactory improvement.

The work of the preceding investigators indicates that the reliability of the results obtained by testing dark adaptation with the biophotometer as a measure of subclinical vitamin A deficiency is not yet established. The chief criticisms of the biophotometer by the investigators mentioned are lack of a fixation point, lack of ability to locate the exact area of the retina being tested and consequent inability to measure rod and cone function separately, the logarithmic relation between the dial settings and illumination, allowing only gross approximations to be made at the bright end of the scale, and the subjective nature of the test which allows the operator no check on the patient's observations. In addition to errors inherent in the instrument, a critical review of the publications mentioned reveals errors of interpretation of data due to a learning factor on the part of the subject and errors due to a lack of sufficient controls.

In the following study a series of patients was tested with the biophotometer, and the data were correlated with the vitamin A content of the blood. The subjects for the most part were patients from the hospital and outpatient department of the Pediatric Service of the Strong Memorial and Rochester Municipal Hospitals. Patients and parents were questioned concerning subjective symptoms of poor dark adaptation, diet, and accessory sources of vitamin A. The physical condition of the patient was known in each case, and patients with fever or acute illness were not included. Subjects exhibiting poor dark adaptation were examined ophthalmologically, and refractive errors were corrected where there was evidence of gross defect.

METHOD

All readings were performed by the same operator on a Frober-Faybor biophotometer in a completely darkened room. The nature of the test was explained and, where necessary, demonstrated to allay any fear on the part of the younger patients. Subjects were kept as comfortable and relaxed as possible during the procedure. Accessory light used was carefully shaded from the eyes. Readings were taken upon entering the dark room, after a ten-minute rest period, twenty seconds by a stop watch after a three-minute period of exposure to a bright light, and every two and one-half minutes for ten minutes. All readings for visual end point were made from lower to higher illumination. Uncooperative subjects were excluded from the series.

STANDARDS

The recommendations suggested by the manufacturers of the instrument were followed in establishing our standard. The reading taken twenty seconds after bleaching was considered the most significant. Readings of 0.6 m.f.c. or less were considered normal; those from 0.6 to 2.0 m.f.c. were considered intermediate; and those of 2.0 m.f.c. or greater, subnormal.

Each series was also regrouped according to the more strict standards suggested by Jeans, where both the postbleaching reading (c) and the final reading (g) are considered. Normal subjects were those with c readings of 0.6 m.f.c. or less and g readings of 0.05 m.f.c. or less; intermediate subjects were those with a c reading of from 0.6 to 1.0 m.f.c., and g readings of from 0.05 to 0.10 m.f.c.; subnormal subjects were those with a c reading of 1.0 m.f.c. or greater, and g readings of 0.10 or greater.

The vitamin A content of the blood was determined by the antimony trichloride method of Carr and Price with some modifications by S. W. Clausen.[28] Almost all of the determinations were made in duplicate, so that it is felt that the results are reliable within the limits of the method. The carotene and xanthophyll were estimated according to the procedure of Clausen and McCoord.[29] The degree of accuracy obtainable and the limitations of the above methods have been considered recently.[30]

The procedure used for the vitamin A absorption test was originated in this laboratory.[31] After a sample of blood had been taken, the child was given by mouth such an amount of a fish-liver oil* that it received 1,520 arbitrary blue units of vitamin A per kilogram of body weight. The oil contained about 210,000 U.S.P. units or 45,600 arbitrary blue units per gram. The latter unit is defined as follows: With the use of a 10 per cent solution of copper sulfate as a standard, a specimen of sufficient content in vitamin A to match the standard when acted upon by the antimony trichloride reagent under the conditions of the test is considered to contain 100 units of vitamin A per 100 c.c.[28] Blood specimens were taken two, four, six, nine, twelve, and twenty-four hours after the administration of the oil. During the test, the child received its regular meals, but cod-liver oil and vitamin A concentrates were omitted from the diet.

RESULTS

Subjects Tested Once With the Biophotometer.—In the first series, ninety-eight subjects were tested once with the biophotometer. One reading was taken after the technique of the test had been explained and demonstrated to each subject. At the time of the reading, a specimen of venous blood was obtained for estimation of the vitamin A, carotene, and xanthophyll content.

The biophotometer readings by the Frober-Faybor standards indicated that thirty-three subjects were in the normal group, sixty-four in the intermediate group, and one in the subnormal group (Table I). The average vitamin A content of the blood was 16.4 units per 100 c.c. for the normal group, and 16.3 units per 100 c.c. for the intermediate group. The one subnormal subject had a vitamin A blood content of 25.4 units

*The authors wish to express their thanks to Dr. Carl Nielsen of the Abbott Laboratories for his kindness in supplying us with the fish-liver oil.

per 100 c.c. When regrouped by Jeans' standards, thirty-two subjects were in the normal group, forty-seven in the intermediate group, and nineteen in the subnormal group. These figures approximate the results previously reported by Jeans. In this grouping the average vitamin A blood content for the normal group is 16.0 units per 100 c.c., for the intermediate group, 17.0 units per 100 c.c., and for the subnormal group, 15.6 units per 100 c.c.

TABLE I

VITAMIN A, CAROTENE, AND XANTOPHYLL CONTENT OF THE BLOOD SERUM IN CHILDREN WITH NORMAL, INTERMEDIATE, AND SUBNORMAL BIOPHOTOMETER READINGS

GROUP	FROBER-FAYBOR STANDARDS				JEANS' STANDARDS			
	NUMBER OF SUBJECTS	CAROTENE μg/100 C.C.	XANTHOPHYLL μg/100 C.C.	VITAMIN A UNITS/100 C.C.	NUMBER OF SUBJECTS	CAROTENE μg/100 C.C.	XANTHOPHYLL μg/100 C.C.	VITAMIN A UNITS/100 C.C.
Normal	33	102.2	54.1	16.4	32	102.5	54.3	16.0
Intermediate	64	93.4	53.2	16.3	47	94.1	53.9	17.0
Subnormal	1	134.0	61.0	25.4	19	95.0	49.8	15.6

The correlation between the vitamin A content of the blood and each biophotometer reading was determined. No correlation was found between any of the seven readings of the biophotometer and the vitamin A content of the blood.

TABLE II

SUMMARY OF CORRELATIONS BETWEEN VITAMIN A CONTENT OF BLOOD AND BIOPHOTOMETER READINGS IN 101 CASES

CONSTANTS FOR VITAMIN A

Mean (m)
for 99 cases = 17.05
for 101 cases = 17.05

Standard deviation (σ)
for 99 cases = 7.60
for 101 cases = 7.50

READING	NO.	m	σ	r
a. Initial	101	0.3421	0.1532	-0.0632
b. After 10′ in dark	101	0.03718	0.0153	-0.0302
c. After 3′ bright light	101	0.8733	0.467	-0.146
d. After 2½′ in dark	99	0.2013	0.0973	-0.0693
e. After 5′ in dark	101	0.08602	0.0490	+0.00826
f. After 7½′ in dark	99	0.05474	0.0285	-0.0923
g. After 10′ in dark	101	0.03916	0.025	-0.0298

In this series it was noted that patients who showed poor biophotometer readings at the first test showed improvement in dark adaptation on subsequent tests after vitamin A therapy was instituted, even though the initial blood vitamin A was not significantly low. Subsequently, it was observed that such subjects showed equally good improvement in dark adaptation on repeated biophotometer readings when no vitamin A therapy was given and no change in diet had been made. The subjects, after repeated tests with the biophotometer, improved up to a

certain level, after which the readings showed a tendency to assume a plateau with no further improvement.

Trained Subjects.—Consequently, a second series of nineteen patients was investigated. Each subject was tested repeatedly with the biophotometer until no further improvement in readings was evident. From eight to ten testings were often needed to accomplish this result. The vitamin A blood content was then determined for comparison with the final biophotometer result. By the Frober-Faybor standards, nine subjects fell in the normal group and ten subjects in the intermediate group; the normal group had an average blood vitamin A content of 17.2 units per 100 c.c., and the intermediate group had an average blood vitamin A content of 13.4 units per 100 c.c. No statistically significant correlation was found between the blood vitamin A values and the post-bleaching biophotometer reading by which the Frober-Faybor standards were determined (Table III).

TABLE III

CORRELATION BETWEEN VITAMIN A CONTENT OF BLOOD AND "C" READING OF BIOPHOTOMETER IN 19 TRAINED SUBJECTS

CONSTANTS FOR VITAMIN A

Mean (m) for 19 cases = 15.22 — Standard deviation (σ) for 19 cases = 6.811

CONSTANTS FOR BIOPHOTOMETER READINGS "C"

READING	NO.	MEAN IN M.F.C.	σ	r
c. After 3' bright light	19	0.6584	0.2604	0.05675

Probable error (ϵ) of r = 0.1479

When the data of these trained subjects were regrouped according to Jeans' standards, nine appeared in the normal group, eight in the intermediate group, and two in the subnormal group. The normal group had an average vitamin A blood content of 17.2 units per 100 c.c., the intermediate group, 12.6 units per 100 c.c., and the subnormal group, 16.7 units per 100 c.c. (Table IV).

TABLE IV

VITAMIN A, CAROTENE, AND XANTHOPHYLL CONTENT OF THE BLOOD SERUM IN CHILDREN WITH NORMAL, INTERMEDIATE, AND SUBNORMAL BIOPHOTOMETER READINGS

Tests Repeated Until Constant Readings Were Obtained

GROUP	FROBER-FAYBOR STANDARDS				JEANS' STANDARDS			
	NUMBER OF SUBJECTS	CAROTENE μg/100 C.C.	XANTHOPHYLL μg/100 C.C.	VITAMIN A UNITS/100 C.C.	NUMBER OF SUBJECTS	CAROTENE μg/100 C.C.	XANTHOPHYLL μg/100 C.C.	VITAMIN A UNITS/100 C.C.
Normal	9	63.6	43.4	17.2	9	63.6	43.4	17.2
Intermediate	10	60.0	39.9	13.4	8	61.3	39.1	12.6
Subnormal	0	-	-	-	2	55.0	43.0	16.7

EFFECT OF TRANSIENT INCREASE OF VITAMIN A CONTENT OF THE BLOOD ON DARK ADAPTATION

Vitamin A absorption tests[31] were performed on ten subjects (Fig. 1). Six subjects showed normal absorption curves with the highest peak for blood values at from four to six hours after vitamin A administration. The average biophotometer postbleaching reading for these subjects showed a transitory improvement in dark adaptation which corresponded with the highest peak for vitamin A blood content.

Four subjects failed to absorb the vitamin A in the usual manner, with the highest level in a relatively flat curve occurring at the eight to twelve hour interval. These subjects showed some improvement in dark adaptation which persisted, suggesting that the vitamin A, being more slowly absorbed, was available for a longer period than in the normal curves.

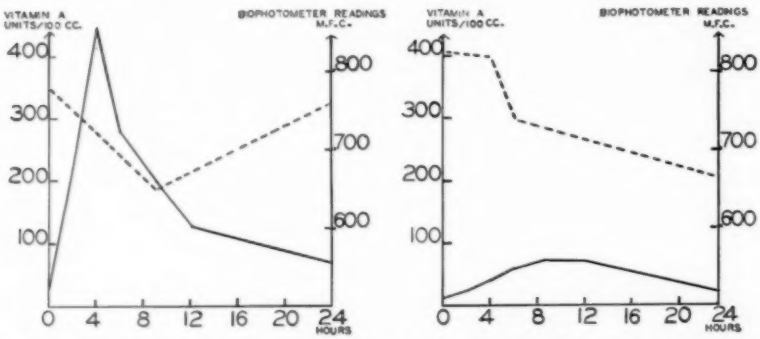

Fig. 1.—*A*, Patients with normal ability to absorb vitamin A; *B*, patients with failure to absorb vitamin A. Solid lines indicate curves for vitamin A; broken lines, curves for biophotometer readings.

These results are based on too few cases to permit any conclusions, but they suggest that there is a transitory improvement in dark adaptation when the blood content of vitamin A is raised significantly for a temporary period.

DISCUSSION

Ninety-eight children were tested once with the biophotometer. In this group, nineteen showed subnormal dark adaptation by Jeans' standards. These results approximate those previously reported by Jeans and would indicate that our biophotometer readings are comparable to his. The more lenient Frober-Faybor standards showed the same normal grouping, but ony one subject had a subnormal reading. Seventy persons from whom dietary history was obtained showed no correlation between diet and biophotometer readings. No history of subjective symptoms of vitamin A deficiency could be elicited from our subjects. Correlation was absent between all readings of the biophotometer and the vitamin A, carotene, and xanthophyll content of the blood.

The question might be raised that in the analysis of the blood all the blue color might not be due to vitamin A. In our laboratory the vitamin A content of the blood by this method has agreed well with the clinical condition of the patient and has shown the expected variations after vitamin A absorption tests. It may be that a single estimation may not give the correct estimation of the supply of vitamin A to the retina. Perhaps in this series there were no actual cases of true vitamin A deficiency. This was considered more probable.

Our experience verifies that of Palmer[20] in regard to improvement in biophotometer readings after repeated testing, due to a probable training factor. In our second series of nineteen trained subjects, several showed improvement on repeated testing without administration of vitamin A. Although about 20 per cent of the untrained subjects were classed as subnormal by Jeans' standards, in the present series of trained subjects only about 10 per cent fell in the subnormal range. Biophotometer readings in this group showed no correlation with blood vitamin A values, but there was a suggestive correlation between the *d*, or first reading of the second test period, and the average carotene content of the blood. This may be of interest in view of Wald's observations[24] that carotene improves dark adaptation in a deficient subject more rapidly than does vitamin A. Our vitamin A absorption curves were too few to permit conclusions.

SUMMARY

No correlation was found between biophotometer readings and vitamin A content of the blood of ninety-eight untrained subjects.

The percentage of subnormal readings approximated that observed by Jeans when our cases were regrouped by his standards.

The decrease in number of subnormal readings found in our series of trained subjects indicates that the training factor is important.

A single reading on the biophotometer is of no value in estimating vitamin A deficiency.

The reading obtained by frequent testing with the biophotometer did not correlate with the blood vitamin A values of our subjects.

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TREATMENT OF RICKETS AND TETANY BY PARENTERAL ADMINISTRATION OF ONE MASSIVE DOSE OF VITAMIN D

HERMANN VOLLMER, M.D.
NEW YORK, N. Y.

TOXICITY OF VITAMIN D

THE question of toxicity of massive doses of vitamin D has arisen repeatedly in discussions and correspondence since the previous publication[1] appeared. The fear that vitamin D has extremely toxic properties has persisted ever since the first reports of pathologic calcifications first in experimental animals[2] and then in children,[3-5] following the use of the old German preparation, vigantol. Vigantol was evidently very toxic. Similar results have been reported also from the use of purer preparations of irradiated ergosterol in animals[6, 7] and from the daily administration of enormous doses, up to 1,000,000 units, of these irradiated products to adults.[8-10] In recent years, only three children[11-13] beyond the first year of life were observed in whom daily administration of doses from 300,000 to 1,500,000 units over a period of weeks caused the appearance of calcium-containing casts in the urine as the sole indication of toxicity.

No toxic manifestations, however, have been reported in rachitic or nonrachitic infants following the administration of one single massive dose of vitamin D_2 or D_3. This is significant since the vitamin D shock therapy of rickets and tetany has been generally accepted in Germany and has been applied to hundreds of infants. I have already found 686 cases published in the medical literature.

The toxicity of irradiated ergosterol is frequently mistaken for the toxicity of crystalline vitamin D_2 or D_3. This error is the source of much confusion. Both products are toxic, like every other chemical substance, in specific doses which vary with the individual. Irradiated ergosterol possesses the toxicity of its vitamin D content augmented by the toxicity of the by-products of the irradiation process.

The irradiation of ergosterol, whether by ultraviolet rays, or ions, or low or high velocity electrons, does not produce vitamin D_2 alone but results in a compound of several irradiation products. As illustrated in Table I, none of them, except vitamin D_2, is antirachitic. On the other hand, some of the antirachitic ineffective irradiation products are toxic, the degree of toxicity rising in the following order: tachysterol, toxisterol, dihydrotachysterol. The latter occurs by reduction of tachysterol, and the amount present is unpredictable. It is identical with the German preparation "A.T.10" of Holtz,[14] which is used for the treatment of tetania parathyreopriva. Dihydrotachysterol increases

From the pediatric service of the Mount Sinai Hospital (chief of staff, Dr. Béla Schick), New York City.

TABLE I

TOXICITY	ANTIRACHITIC EFFICACY	PROVITAMINS AND THEIR IRRADIATION PRODUCTS				
none	none	ergosterol	7-dehydrocholesterol	22-dihydroergosterol	7-dehydrositosterol	7-dehydrostigmasterol
none	none	lumisterol$_2$	lumisterol$_3$		lumisterol$_5$	
slight	none	tachysterol$_2$	tachysterol$_3$			
marked	none	dihydrotachysterol (A.T. 10)				
1:3000-3500	marked	vitamin D$_2$	vitamin D$_3$	vitamin D$_4$ (½ efficacy of D$_2$)	vitamin D$_5$ (1/40 efficacy of D$_2$)	vitamin D$_6$ (1/250-400 efficacy of D$_2$)
marked	none	toxisterol				
none	none	suprasterols I and II	(suprasterols not isolated)			

the calcium level of the serum and is probably responsible to a great extent for metastatic calcifications ascribed to overdosage of vitamin D. Widenbauer[15] has found that most symptoms of the so-called D-hypervitaminosis can be produced by overdosage of dihydrotachysterol.

Vitamin D_2 has been isolated from the other irradiation products by repeated crystallization. It is practically free from toxic by-products, but is toxic itself when administered in enormous dosage. Its therapeutic index, i.e., the relation between its toxic and antirachitic effect, is according to Göttche[16] 1:3,500, and according to Laquer and Linsert[17] 1:3,000. In impure irradiation compounds, this relation has been established by Göttche[16] to be 1:2,380. This means according to C. Bomskov[18] that only 3,000 to 3,500 times the effective antirachitic dose of vitamin D_2 when administered ten times within twelve days, produces toxic manifestations. If 1,000 units of vitamin D_2 are regarded as the lowest effective dose for infants, only a dose of 3,000,000 to 3,500,000 units will produce toxic symptoms. This is far beyond the dosage applied in the vitamin D shock therapy or prophylaxis; 600,000 units of vitamin D_2 is about one-fifth of the toxic dose, and, when given only once, is far below the limits of risk.

The same is true for crystalline vitamin D_3, for cod-liver oil and fish-liver oil concentrates when given in the same dosage. Fish-liver oils do not contain any of the toxic products which occur with the irradiation of provitamins. Vitamin A, simultaneously administered with vitamin D in fish oil is supposed to counteract possible vitamin D toxicity (Thoenes,[119] Jusatz[20]).

The danger of toxicity is further diminished by the facts that only one massive dose of vitamin D is required, instead of ten doses within twelve days (Bomskov[18]), and that it is given to a rachitic patient. The tolerance of a rachitic infant to vitamin D is definitely higher than that of a nonrachitic adult. The fact that a rachitic patient retains about 97 per cent[21] of 600,000 units of vitamin D, administered in one single dose, indicates that there is an actual need for this dosage to refill the depleted tissues.

These theoretical explanations have been confirmed by practical experience. One hundred fifty-eight children received single massive doses of vitamin D, for various clinical purposes. Various irradiation compounds as well as pure crystalline vitamin preparations were used and administered orally or intramuscularly. In most cases the dose was 600,000 units of vitamin D; only a few children received doses between 250,000 and 500,000 units. The age range was between premature infants in the first weeks of life and 16-year-olds. Nonrachitic as well as rachitic and tetanic children were treated. In no instance did any clinical sign of toxicity occur. Calcium-containing casts were never found in the urine.

PARENTERAL ADMINISTRATION OF VITAMIN D

In the previous publication,[1] the oral administration of a massive dose of vitamin D was recommended as the method of choice, and the parenteral application reserved for certain purposes. The oral method is satisfactory for the treatment of hospitalized children. In clinics, in private practice, and particularly in a general prophylactic campaign, it would be cumbersome and almost impossible for the physician to take care of administering the proper dose to every individual child. This procedure would be automatically left to the mother or nurse, thus bringing about many factors of uncertainty and endangering the result. The vitamin may not be given at all; this would be more serious than the omission of one or two doses in the routine therapy and prophylaxis with repeated small doses of vitamin D. If the massive dose is incorporated in milk, as it should be, the infant may refuse to drink the whole bottle. Since the oily solution of vitamin D is found on the surface of the milk, the greater part of the vitamin would be discarded with the remainder of the milk. When given without milk, a great deal of the oily solution of vitamin D is not absorbed, according to the observations of F. Küster.[22] Even if the vitamin D is quantitatively fed with milk, the infant may vomit, or the vitamin may not be completely utilized in case an oil diarrhea develops.

All these eventualities are eliminated when the massive dose of vitamin D is administered parenterally. At least a general prophylaxis of rickets should be based, for safety's sake, on this method which avoids the high percentage of failures encountered with the routine method of prophylaxis.[23, 24] Like smallpox vaccination, rickets prophylaxis should lie in the physician's hand, and be performed by one single manipulation which is as foolproof as possible.

One massive dose of vitamin D can be injected in oily solution. Slow absorption results, and the viscosity of the oily solvent necessitates the use of wide-borne needles, which cause pain. In cases of active rickets as well as cases of manifest or latent tetany, quick absorption and action of the vitamin D is desired. The oily solution does not meet these requirements.

The speed of absorption of a drug in oily solution which is injected intramuscularly depends chiefly on the extent of surface contact between the oily vehicle and the tissue and the solubility of the drug in the tissue. Both factors are favored by the addition of ether to the oily vehicle. Ether decreases materially the viscosity of the oil. This alteration of the viscosity does not take place proportionally in direct ratio to both constituents, but follows a hyperbolic curve. Relatively small amounts of ether therefore reduce the viscosity of oil to a fraction of its original viscosity. Consequently the mixture of oil and ether, in contrast to oil alone, spreads immediately after the injection, and forms a large contact

surface with the tissues. Many more interstices of the muscle come in contact with vitamin D carried in a thin vehicle. In the muscle interstices, according to Nernst's law of distribution, the following equilibrium develops:

oil ether vitamin D	→ vitamin D ether →	vitamin D ether cell sterols and fats

Since vitamin D is much more soluble in ether than in oil, the ether carries vitamin D to the cell sterols and fats where the vitamin is absorbed. In this way, the absorption of vitamin D can be rapid in comparison with that of the oil which may remain in situ for months.

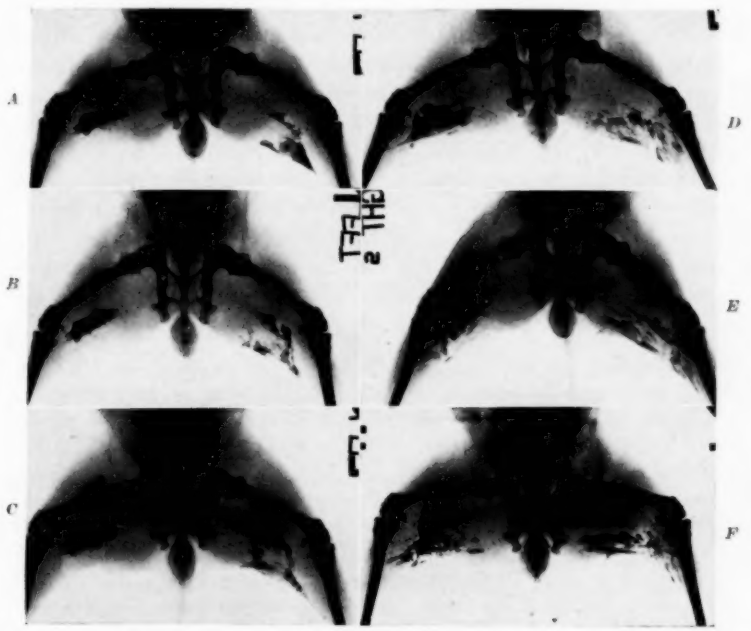

Fig. 1.—The immediate and wider spread of an intramuscularly injected mixture of oil and ether (on the right side of each film) as compared with oil alone (on the left side). The x-rays are taken at the following times after the simultaneous injection of both solvents:
A, 5 seconds; *B*, 15 minutes; *C*, 1 hour; *D*, 24 hours; *E*, 4 days; *F*, 13 days.

The difference in extent and absorption of oil, and a mixture of oil and ether in muscle has been shown by the following experiment: Symmetrical muscle sites of a rabbit were injected simultaneously with 1.0 c.c. of iodochlorol, on one side, and 0.6 c.c. of iodochlorol and 0.4 c.c. of ether on the other. Iodochlorol is an iodized oil and was chosen for better x-ray visualization. X-ray films were exposed immediately after injection (Fig. 1, *A*), 15 minutes (Fig. 1, *B*), 1 hour

(Fig. 1, *C*), 24 hours (Fig. 1, *D*), 4 days (Fig. 1, *E*), and 13 days (Fig. 1, *F*) later. They demonstrate clearly the relatively wide spread of the oil-ether mixture as compared with the oil alone, which does not show any spread within one hour and almost none after 24 hours. Thirteen days after the injection, there are still on both sites remainders of oil. As Schick and his co-workers[25] and Binet[26] have previously observed, injected oil may remain in situ for months. This does not rule out, however, the absorption of the substance diluted in the oil, as demonstrated by Binet.[26]

Peanut oil was chiefly used as a carrier for vitamin D because it seemed to be less irritating and seemed to cause fewer allergic reactions than other vegetable oils. The following proportions of the three constituents were found the most suitable for intramuscular injection: 600,000 units of vitamin D, 0.6 c.c. of peanut oil, and 0.4 c.c. of ether.

This mixture is thin enough to pass through hypodermic needles. Consequently, the intramuscular injection causes little or no pain, an additional clinical advantage. The solution was sterilized for 3 minutes at 100° C. This temperature does not affect the vitamin D, as was shown in previous studies. Probably because of the germicidal effect of ether, the solution was found to be sterile without sterilization by heat and was used without heat sterilization in later experiments. In no instance was any infiltration observed after the intramuscular injection of this solution.

CLINICAL OBSERVATIONS

It remained to be proved that vitamin D is actually as quickly absorbed and as effective when given parenterally in peanut oil and ether as when administered orally. This could only be demonstrated in children with active rickets or tetany. Figs. 2 to 9 contain all the pertinent facts.

CASE 1.—Carol Z., 2-week-old infant with neonatal tetany and general convulsions, received 500,000 units of vitamin D_2 parenterally as the only form of treatment. Serum calcium rose from 7.8 to 10.9 mg. per cent, and the convulsions did not recur after vitamin D shock therapy. (Fig. 2.)

CASE 2.—Eleanor V., a 10-day-old infant with neonatal tetany, developed general convulsions on the eighth day of life, positive Chvostek sign, serum calcium, 6.4 mg. per cent. Calcium gluconate intravenously, calcium lactate by mouth, and two injections of parathormone did not influence the clinical picture, but raised the serum calcium to 8.5 mg. per cent. The striking effect of 600,000 units of vitamin D_2 can hardly be ascribed to the parathormone which was given two days earlier. (Fig. 3.)

CASE 3.—Lucy P., a 15-month-old child with scurvy and active rickets. Following the intramuscular administration of 600,000 units of vitamin D_2, serum calcium and phosphorus became normal within 3 days. Roentgenographic evidence of healing appeared first after 8 days, was advanced after 14 days, and was complete after 30 days. (Fig. 4.)

CASE 4.—Robert P., a 4-month-old white premature infant whose birth weight was 4 pounds, and who developed moderate rickets. Serum calcium was 8.3, phosphorus 3.2 mg. per cent. Intramuscular injection of 600,000 units of vitamin D_2 raised serum calcium and phosphorus to normal within 6 days, and quick healing

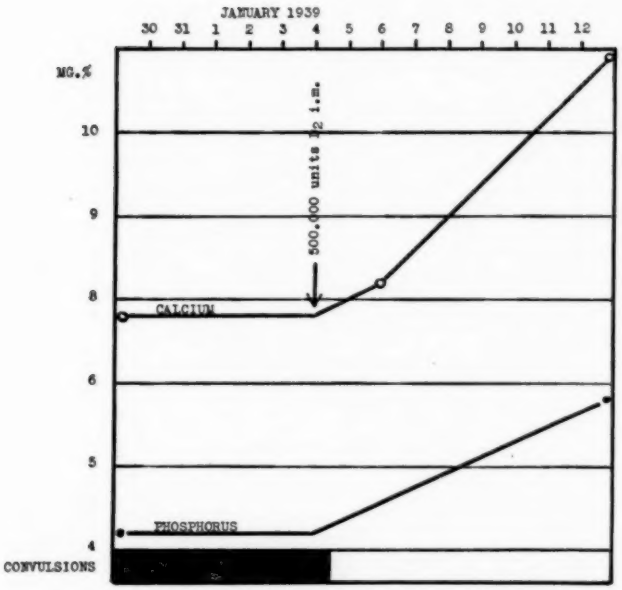

Fig. 2.—Case 1.

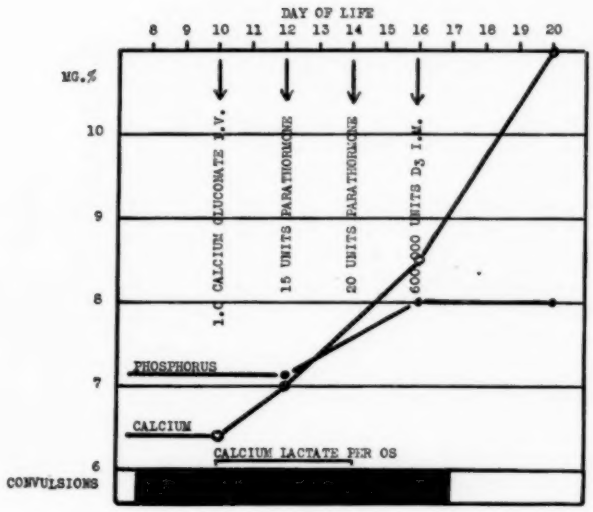

Fig. 3.—Case 2.

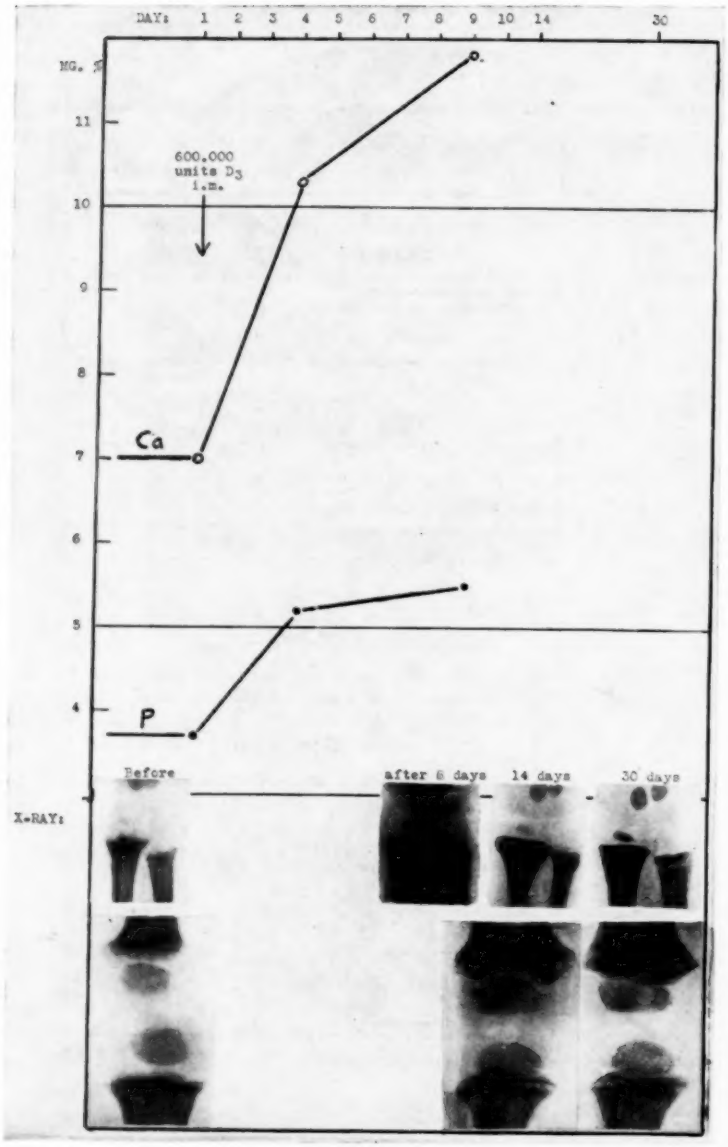
DAYS
1
2
3
4
5
6
7
8
9
10
14
30
MG. %
11
10
9
8
7
6
5
4
600,000
units D3
i.m.
Ca
P
Before
after 6 days
14 days
30 days
X-RAYS

Fig. 4.—Case 3.

of the rachitic process followed. X-ray examination showed complete calcification 28 days after the injection of vitamin D_2. (Fig. 5.)

CASE 5.—John D., a 4-month-old colored infant with bronchopneumonia, marked craniotabes, enlarged epiphyses, and rosary. The phosphatase was 148 King-Armstrong units, indicating the presence of active rickets in spite of a high serum phosphorus, which may be ascribed to the bronchopneumonic process.

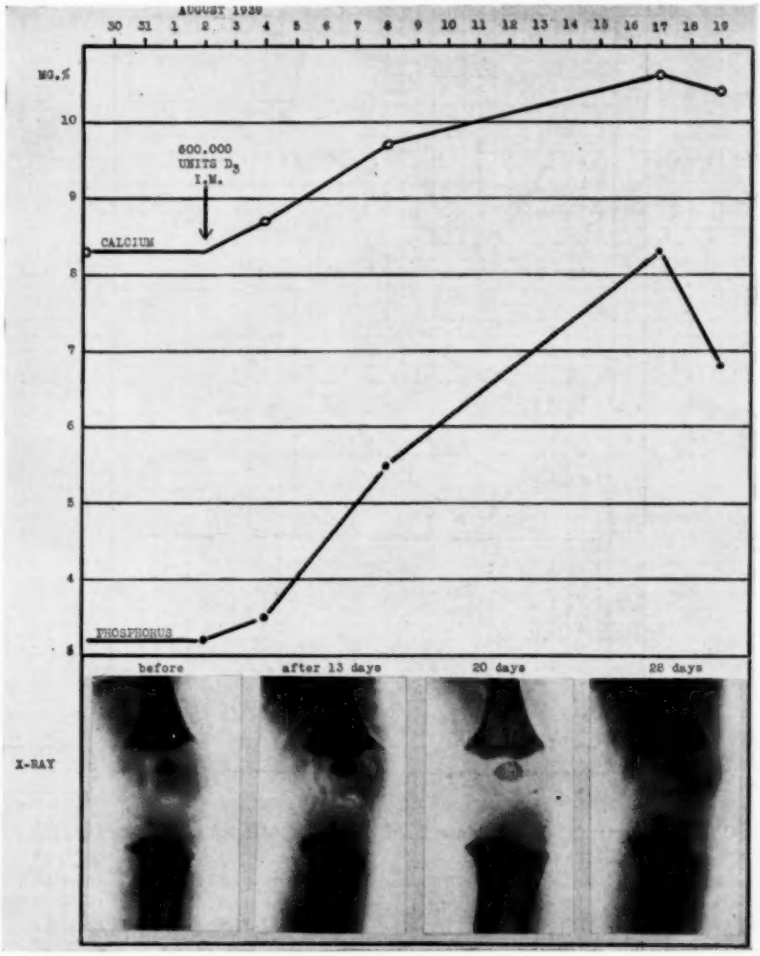

Fig. 5.—Case 4.

When the pneumonia had subsided, serum phosphorus was 4.1 and calcium 8.0 mg. per cent. Intramuscular injection of 600,000 units of vitamin D_2 increased serum phosphorus to 5.9, and calcium to 9.8 mg. per cent within 6 days. The craniotabes disappeared 10 days after this treatment. (Fig. 6.)

CASE 6.—Ferdinand G., a 9-month-old Puerto Rican infant with slight scurvy and active rickets. Serum phosphorus was 3.5 mg. per cent; calcium, 10.5 mg. per

cent; phosphatase, 41 King-Armstrong units before the treatment. X-ray examination at this time seemed to show a chronic "intermittent" rickets in an active phase. A massive dose, 600,000 units, of vitamin D_2 raised serum phosphorus and calcium to normal, and caused progressive recalcification of the bones which was almost completed 30 days after vitamin D shock therapy. (Fig. 7.)

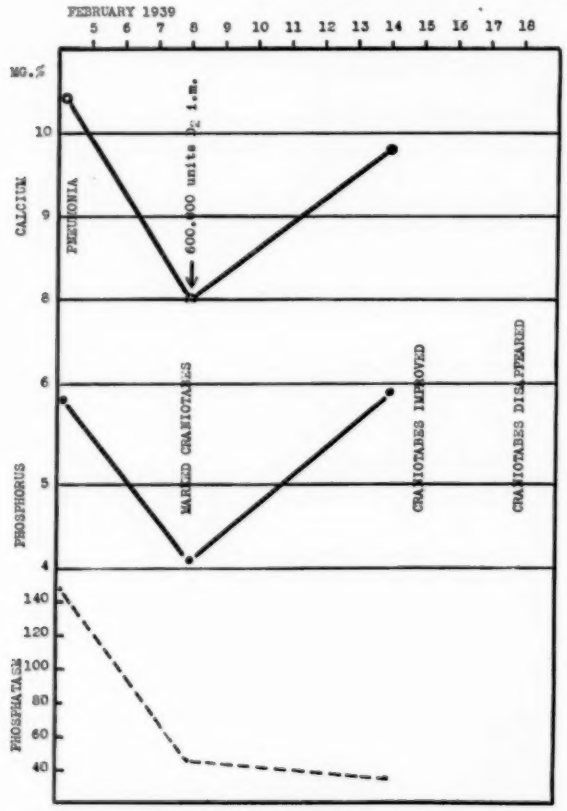

Fig. 6.—Case 5.

CASE 7.—Gertrude O., a 6-month-old colored dystrophic infant with rickets, markedly enlarged liver and spleen, and severe hemolytic anemia. Serum phosphorus was 3.2 mg. per cent; serum calcium, 9.8 mg. per cent; and serum phosphatase, 41.5 King-Armstrong units. Intramuscular administration of 600,000 units of vitamin D_2 influenced the blood chemistry definitely but slowly. After 22 days, phosphorus had risen from 3.2 to 4.5 mg. per cent, and only after 45 days rose to 6.3 mg. per cent, with a serum calcium of 11.6 mg. per cent. Meanwhile roentgenographic evidence of healing rickets became distinct after 16 days, and complete after 44 days following the treatment. (Fig. 8.)

In this case the healing process was obviously delayed as compared with other cases. In addition, this infant developed rickets in spite of a daily intake of 2 teaspoonfuls of cod-liver oil which were given regularly for the three months prior to admission. On admission the infant showed severe anemia, a

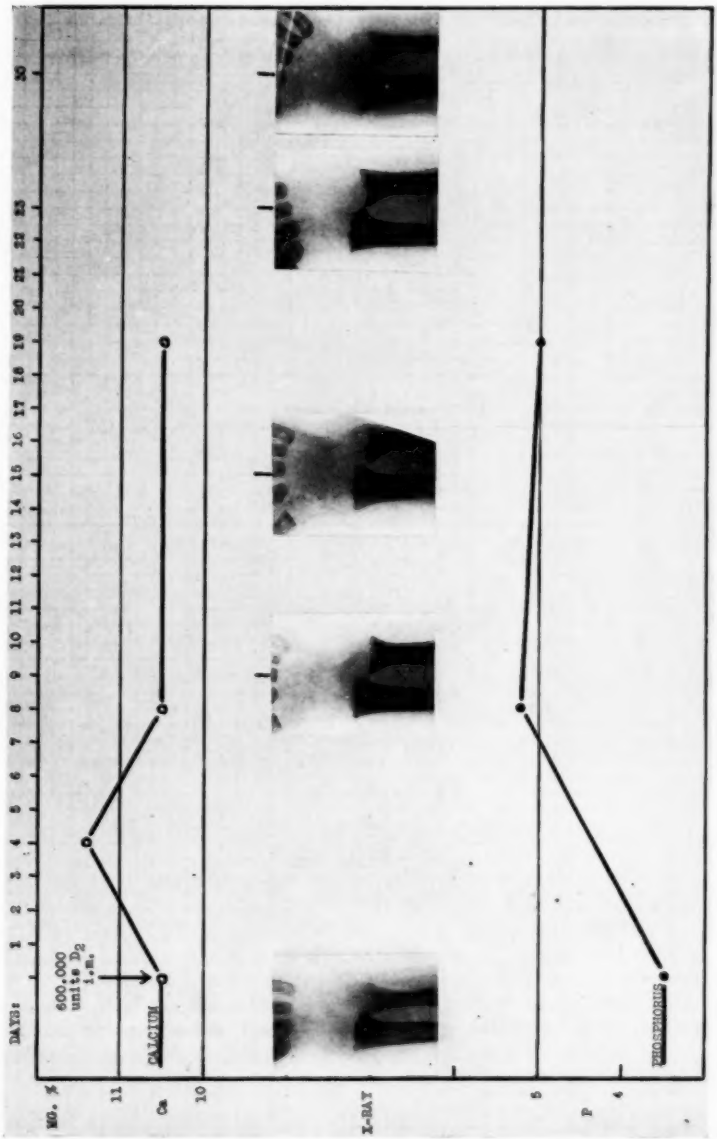

Fig. 7.—Case 6.

markedly enlarged liver, and a positive Takata-Ara reaction, suggestive of liver damage. This may explain the lack of response to the previous oral treatment with cod liver oil as well as the complete but delayed curative effect of the parenteral vitamin D_2 administration.

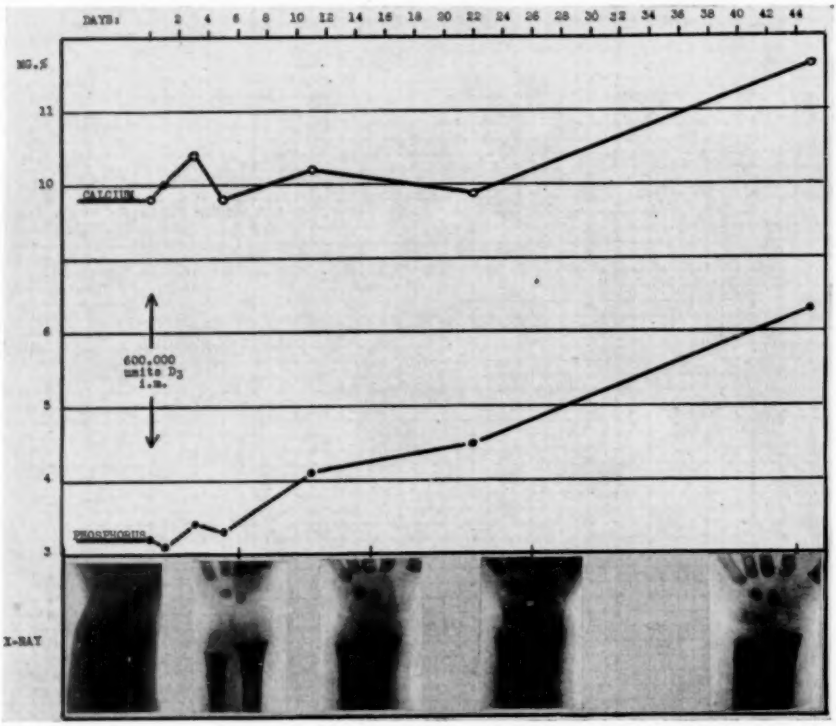

Fig. 8.—Case 7.

CASE 8.—Elaine S., a 6½-year-old white girl with severe rickets of the Fanconi[27] type, characterized by severe rickets, dwarfism, hypophosphatemia, glycosuria, albuminuria, acidosis, and the excretion of large amounts of organic acids in the urine. The child received 2,200,000 units of vitamin D by mouth within three weeks. Serum phosphorus and calcium were raised only temporarily following the administration of the first massive dose of vitamin D, only to drop down again to their original levels, until further repeated massive doses of vitamin D were given. Only slight calcium deposition could be seen in the roentgenograms of the wrist, 32 days after the beginning of the treatment with repeated massive doses. (Fig. 9.) The child was transferred to another hospital before the parenteral administration of vitamin D could be tried.

COMMENT

The parenteral administration of one massive dose of vitamin D in a solvent of oil and ether has been shown to have the same effect on rickets and tetany, and to act as quickly, as the same doses of vitamin D when administered by mouth. Serum calcium and phosphorus

become normal usually after three to seven days. The calcium deposition in the bones makes its first roentgenographic appearance usually at the end of one week, proceeds rapidly, and is usually complete thirty days after the beginning of the treatment. Tetanic convulsions cease within 24 hours after the parenteral administration of one massive dose of vitamin D.

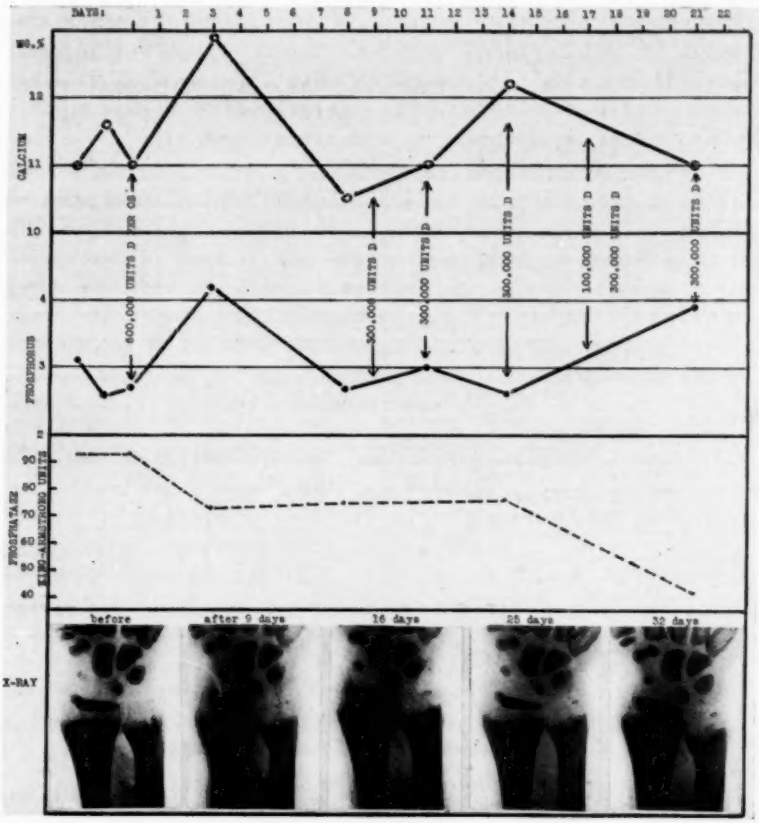

Fig. 9.—Case 8.

No difference was observed between the effect of vitamin D_2 and D_3. If there is any, it can rather be demonstrated by a minimum dose therapy than by the massive dose treatment.

Parenteral administration of 600,000 units of vitamin D caused neither local infiltration nor evidence of systemic damage. No calcium-containing casts were found in the urine.

Once the efficacy and harmlessness of the parenteral vitamin D shock therapy were ascertained, the parenteral vitamin D prophylaxis could be tried. This has been done successfully, in cooperation with

C. Zelson, in a large number of premature infants, as will be shown in a separate communication.

SUMMARY

The harmlessness of one single dose of 600,000 units of vitamin D is shown theoretically and is practically demonstrated by its administration to 158 children in whom no toxic manifestations occurred.

The parenteral administration of one massive vitamin D dose is recommended for certain clinical purposes. The absorption of parenteral vitamin D depots can be accelerated by using a mixture of oil and ether instead of oil alone as solvent. The superiority of an oil-ether mixture in this respect is demonstrated by animal experiment.

Rickets and tetany respond to this form of parenteral vitamin D shock therapy as promptly as to the oral administration of equal doses of vitamin D. Serum calcium and phosphorus become normal usually after three to seven days. Roentgenographic evidence of calcification shows within one week, and recalcification is usually complete thirty days after the beginning of the treatment. Tetanic convulsions cease within 24 hours after the parenteral administration of one massive dose of vitamin D.

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25 Central Park West

AN EVALUATION OF A HEALTH PROGRAM FOR FOSTER HOME CHILDREN IN AN INDUSTRIAL COMMUNITY

J. A. JOHNSTON, M.D., AND P. J. HOWARD, M.D.
DETROIT, MICH.

IN ATTEMPTING to evaluate health measures and their effect on mortality, there arises constantly the difficulty of distinguishing between immediate and remote causes of death, between specific disease processes and underlying factors which may condition the outcome of a given disease process. It will be generally conceded that the reduction in mortality from diphtheria, typhoid, small pox, and malaria results from the application of specific measures, while, to a large extent, it is quite generally felt that the diminished incidence of and mortality from the acute gastroenteric illnesses of the summer months relates, not so much to any improvement in the specific management of the illness when it has developed, nor to a very large extent from an elimination of specific causative organisms, but rather to a general improvement in infant nutrition preceding the onset of the hitherto fatal illness. The same clinical impression is reasonably well founded in the case of bronchopneumonia; the outcome is conditioned to a large extent, not by the employment of specific therapeutic measures, but by the nutritional state of the child infected. In the case of tuberculosis, this thesis lacks proof, but it is the expressed opinion of the League of Nations committee on nutrition that the continued high incidence of the adult and fatal forms of this disease in persons of the 'teen ages can be attributed to an impairment of nutrition resulting from a variety of causes which have in common a suboptimal dietary, implying that the transition from the childhood to the adult type occurs in a certain percentage of cases, not from contact reinfection, but as a result of endogenous reinfection.

Data on the worthwhileness of an "improved general state" are difficult to obtain and equally difficult to evaluate, and for this reason it is felt that the experience of twenty years with a large group of children from the lower economic strata in an industrial center might be worth recording as bearing on this point.

The Child Caring Department of the Society of St. Vincent de Paul of Detroit employs the foster home system in caring for its wards. These are assigned to its care in large part by a legal agency following the rupture of the family group, in some instances, as a result of economic difficulty, but in as many instances, as a result of disease such as tuberculosis, in the family. The foster homes are in thirty suburban communities near Detroit, though a small number are maintained in the city in which are placed those children assigned to special schools or requiring frequent clinic visits. During the first nine years under consideration, excellent medical care of the children was available in the clinic and hospital but was given for specific illness. During the latter

From the Henry Ford Hospital.

eleven years a system was employed which involved the following routine: On admission to the care of the Society, each child was entered as an inpatient at the Henry Ford Hospital where he remained as long as seemed necessary to permit his discharge as normal. The routine physical appraisal included an evaluation of nutrition, a search for and

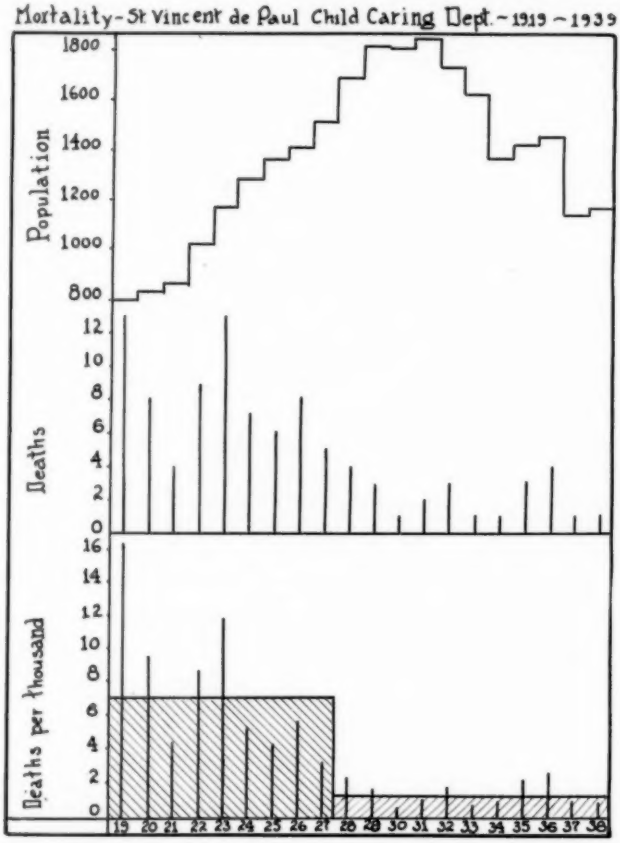

Fig. 1.—The crosshatching in the bottom graph represents the average of the number of deaths per thousand in the two periods—the nine years preceding the Henry Ford Hospital arrangement, and the eleven years since that plan was adopted.

removal of foci of infection, which included tonsillectomy, adenoidectomy, and the extraction of diseased teeth when indicated, refraction, tuberculin testing and x-ray examination of reactors, and Wassermann and Schick tests. A mental appraisal by a psychologist and psychiatrist was done when indicated. Immunization against diphtheria and smallpox was given during the stay. Infants under 1 year of age were kept only long enough to demonstrate the adequacy of their feedings and then placed in urban homes where intimate supervision by a visitor was

possible at frequent intervals. Intercurrent illness was promptly treated by hospitalization.

A special plan has been followed in the cases of two groups of patients, which we think has likewise contributed to the end results. All reactors to tuberculin and all children who had been exposed to tuberculosis whether or not they proved to be reactors, are followed in a special clinic to which they return at least once a year for general check and x-ray examination. This has not prevented the occurrence of what we interpret as endogenous reinfection, but the adult type cases, thirty-two in number, are picked up in this way at such an early stage that we feel mortality has definitely been affected thereby. Because so high a percentage of reinfection type of tuberculosis is found in the adolescent girl, provision for this group has been made in a summer camp operated by the Society. The children with congenital syphilis are likewise cared for in a special clinic, and the end results in their case are reported in another communication by one of us.[1]

Between 1919 and 1939 the Child Caring Department has had under its care 27,374 children as a running population, or an average of 1,368 per year. The mortality during this period has shown a striking decline, and while much of this is a reflection of the same trend in the community at large, the difference between the two periods being compared is out of proportion to this expected trend and seems significant enough to be related to the changed program adopted in 1927. The details of this decline in mortality appear in Table I and Fig. 1. The average

TABLE I

MORTALITY IN CHILD CARING DEPARTMENT OF SOCIETY OF ST. VINCENT DE PAUL, 1919-1938

YEAR	YEARLY POPULATION	NUMBER OF DEATHS	RATE PER 1,000
1919	800	13	16.2
1920	836	8	9.5
1921	874	4	4.5
1922	1,027	9	8.7
1923	1,172	13	11.9
1924	1,291	7	5.2
1925	1,371	6	4.3
1926	1,408	8	5.6
1927	1,524	5	3.2
Total	10,303	73	7.1
1928	1,693	4	2.3
1929	1,825	3	1.6
1930	1,824	1	0.5
1931	1,837	2	1.0
1932	1,741	3	1.7
1933	1,617	1	0.6
1934	1,364	1	0.73
1935	1,417	3	2.1
1936	1,451	4	2.6
1937	1,142	1	0.87
1938	1,160	1	0.86
Total	17,071	24	1.4

It is realized that the figures for years of child care would be more valuable if expressed as months of child care, but the information is not available in the control groups.

age of the children in the groups before 1927 and after 1927 was the same. In the early years, medical care was given in whatever community the child happened to be boarding, and records of the cause of death were not consistently available; accordingly, the comparison of the causes of death loses some force, but this in no way invalidates the contrast between the two sets of mortality rates.

TABLE II

MORTALITY IN COMPARABLE GROUPS OF FOSTER HOME CHILDREN FROM CHILD CARING SOCIETIES IN MICHIGAN

YEAR	POPULATION OF CHILD CARING INSTITUTIONS	TOTAL DEATHS	DEATHS PER 1,000
1920	4,138	20	4.8
1921	4,080	36	8.8
1922	3,945	22	5.5
1923	3,842	33	8.5
1924	3,809	24	6.3
1925	3,975	23	5.7
1926	3,790	20	5.2
1927	3,941	13	3.2
1928	6,127	29	4.7
1929	6,220	41	6.5
1930	6,231	31	4.9
1931	5,993	13	2.3
1932	5,667	14	2.4
1933	5,093	9	1.7
1934	4,753	37	1.4
1935	5,374	14	2.6
1936	21,514*	96	4.5*
1937	21,820*	86	3.9*

*Includes groups from Pittsburgh, Chicago and Buffalo.

For comparative purposes attempt has been made as shown in Table II to obtain figures on comparable age groups of wards of child caring agencies, including groups housed in institutions and in foster homes in Chicago, Pittsburgh, Buffalo, and Michigan. It was interesting to note among the reports some such statement as "the child seemed malnourished and weak when brought under care and later died of pneumonia"; but it is equally striking to note the low figures of recent years for this group.

TABLE III

MORTALITY FROM THREE PRINCIPAL CAUSES OF DEATH IN CHILDREN BEYOND THE NEWBORN GROUP

YEARS	GROUP	YEARLY POPULATION	RESPIRATORY INFECTION		GASTROENTERIC ILLNESS		COMMUNICABLE DISEASE	
			NO. OF CASES	RATE PER THOUSAND*	NO. OF CASES	RATE PER THOUSAND*	NO. OF CASES	RATE PER THOUSAND*
1920 to 1929	Control	32,175	77	2.2	67	2.0	32	0.9
	St. Vincent	4,916	10	2.0	6	1.2	7	1.4
1930 to 1938	Control	24,836	27	1.9	14	0.5	6	0.25
	St. Vincent	17,071	3	0.2	2	0.1	1	0.05

*Rate per thousand children cared for during one year.

There are listed in Table III the data on the three principal causes of death in this age group which exeludes the newborn period.

In Table IV are tabulated the causes of all deaths in the second phase

TABLE IV

CAUSES OF DEATH

CAUSE OF DEATH	1919-1927	1928-1938
Respiratory infection	11	3
Early infancy death	1	0
Gastroenteritis	9	2
Malformations	3	0
Communicable disease		
Diphtheria	5	1
Measles	1	0
Pertussis	1	0
Accidents	1	4
Appendicitis	4	2
Syphilis	2	0
Streptococcus sepsis	1	1
Nephritis	1	1
Meningococcus meningitis	2	0
Tuberculosis	2	3
Ulceration of esophagus	0	1
Cerebral hemorrhage	0	1
Hodgkin's disease	0	1
Acute intestinal obstruction	0	1
Bargen's bacillus colitis	0	1
Anesthetic death	0	1
Unascertainable	29	0
Total	73	23

of the care of the children, but their comparison with those in the first phase is of course inaccurate because of the incomplete data.

SUMMARY

The mortality was studied in a group of 27,374 children over a twenty-year period and a comparison was drawn between a program in which were stressed prophylaxis and constant attention to an improved general state and one in which medical care was given chiefly during illness. A striking decrease in mortality was demonstrated, which was greater than could be attributed to the improvement noted in the figures for the population at large and for similar groups of wards of charitable agencies.

REFERENCE

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AN EIGHT-YEAR SURVEY OF A TUBERCULOSIS CONTROL PROGRAM AMONG NONCONTACT INFANTS AND YOUNG CHILDREN

ANTOINETTE RAIA, M.D., AND HUGH CHAPLIN, M.D.
NEW YORK, N. Y.

THE East Harlem Nursing and Health Service of New York City provides health supervision for the infants and preschool children of a district with approximately 60,000 population, of whom from 60 to 70 per cent are on home or work relief. An average of 500 new infants are registered annually. All ante-partum and post-partum supervision and all sick calls in the district are provided for by the nurses of the Service. Four medical clinics and two nurses' conferences are held each week at its headquarters. It is evident, therefore, that close contact is kept both at the clinics and in the homes with the Service clientele.

Since 1931 the routine use of the Mantoux test has been part of the health supervision provided at the East Harlem Nursing and Health Service. The results of eight years of this program (September, 1931, to September, 1939) have been tabulated and analyzed and are now offered as another effort in the general popularizing of the Mantoux test.

The age period studied includes the infant and preschool groups. Our routine is to administer the Mantoux test when an infant reaches 1 year of age. New patients who are admitted to the clinic at a later age are given the test on admission or shortly thereafter. The dosage employed is 0.1 mg. of the New York Department of Health preparation of old tuberculin. The test is given intracutaneously on the forearm and read at the end of forty-eight hours. The areas of induration and erythema are indicated by measuring the two diameters; they are recorded as *one plus* if the reading is less than 1 cm., *two plus* if it is between 1 and 2 cm., and *three plus* if it is greater than 2 cm. A *four-plus* reaction is ascribed to any test in which vesiculation takes place. If the reaction is negative, the test is repeated at yearly intervals. It is not repeated again once it becomes positive. Every child with a positive Mantoux test is x-rayed, the family is instructed in the significance of tuberculosis, and the members of the family are urged to be examined in an attempt to find the source of infection. Special efforts are immediately made to provide the child with additional food, vitamins, and rest periods. Country care and preventoria are utilized as the case requires. It has

From the East Harlem Nursing and Health Service of New York City.

been found necessary, because of poor home conditions, to send the majority of cases with x-ray evidence of disease to sanatoria. An attempt has been made to prevent the occurrence of contagious diseases and acute respiratory infections. Further efforts along these lines are contemplated.

These infected children are kept under supervision by periodic physical and x-ray examinations on the average of once or twice a year, or more frequently when indicated. This period of observation will extend, so far as it is possible, through and beyond the adolescent years. Although the follow-up of these children has several functions, such as the maintenance of optimum health, the tracing of all possible leads in discovering the source of infection, and the education of the family, its ultimate objective is the discovery of chronic pulmonary tuberculous lesions (reinfections) in the earliest possible stage. We are aware that x-rays during the childhood period are not infrequently negative in an appreciable percentage of positive reactors, but it is felt that better cooperation can be obtained from these children when they reach puberty if the association with the health center remains unbroken through the childhood years.

From the medical standpoint, an analysis of the figures revealed the facts given in Tables I, II, and III.

TABLE I

TOTAL TESTS PERFORMED AND RESULTS OBTAINED

Total number of children tested	4,841	
Negative reactors	4,493	
Positive reactors	348	(7.2%)
Total number of tests performed	7,530	
Negative reactions	7,182	
Positive reactions	348	(4.6%)

Table I shows that a tuberculous infection was discovered in 348 children, which would have been undetected otherwise because of the absence of a suggestive history. Thus, this routine procedure of tuberculin testing all children in this health center supplements the work of the City Department of Health, which supervises only those children exposed to reported cases of tuberculosis.

TABLE II

RESULTS OF ANNUALLY RETESTING PREVIOUSLY NEGATIVE REACTORS

NUMBER OF TIMES TEST PERFORMED	1	2	3	4	5	6
Number of children tested	4,841	1,723	704	209	47	6
Number found positive	236	82	27	3	0	0
Percentage positive	4.8	4.7	3.8	1.4	0	0
Positive reactors discovered within one year from onset of infection as result of retesting annually		112				

Table II shows the value of retesting in the early discovery of new cases of tuberculous infection. As a result of retesting, in some instances as often as six times, 112 cases were discovered within one year from the onset of infection. In this manner, important measures could be instituted early in the care of the child, especially as regarded his removal from the source of infection.

Of the 348 patients who reacted positively, 203 are being carried by the clinic, the remainder having moved away or having transferred to other care. A study of these 203 cases reveals that 22, or 10.8 per cent, were in the important infant age group where the seriousness of the disease is well recognized. The x-ray revealed evidence of tuberculosis in twenty-one instances (10.3 per cent), four of which were in infants. Ten of these twenty-one cases had lesions characteristic of active primary tuberculosis; ten showed calcifications, either in the parenchyma or lymph nodes or both; and one case had a reinfection type of tuberculosis of minimal extent. This child had a positive Mantoux reaction at the age of 5 years. Yearly x-rays had been negative until the age of 9 years when a routine x-ray revealed an infiltration in the first left anterior interspace. The parents and siblings were examined and found free from disease. The child was put to bed, and after fourteen months she was able to return to school, and, to date, has done well for a period of one year.

In an attempt to find the sources of infection in these 203 cases, we were able to secure examinations of 61 fathers and 83 mothers, making the total of parents examined 144, or 35.6 per cent, of all parents. The x-rays of these parents were negative with the exception of those of four mothers and one father in whom lesions of pulmonary tuberculosis were found, two of which were active and three apparently arrested. Carrying the investigation further, sources of infection were found outside the family in an additional forty-one persons. These included relatives, friends, neighbors, and boarders. By these efforts, the source of infection was thus discovered in 46 (22.6 per cent) of the 203 children with positive Mantoux reactions.

It is interesting to note that the disease of fifteen of these forty-six adults with pulmonary tuberculosis had not been known prior to the investigation by the East Harlem Nursing and Health Service. None of the children in our study presumably infected by the remaining thirty-one adults with pulmonary tuberculosis already known to the Department of Health had been examined. This was due to the fact that the infected child was not in the immediate family of the registered positive case, or that he was not in the family at all, but merely a close neighbor.

This particular effort in seeking the possible sources of infection in these 203 children shows the manner in which different types of tuberculosis case finding investigations can supplement each other. Those organ-

TABLE III

SUMMARY OF X-RAY FINDINGS, EXAMINATIONS OF PARENTS, SOURCES OF INFECTION, AND SIZE OF MANTOUX REACTIONS

DATE	CASES CARRIED			X-RAY FINDINGS						PARENT EXAMINATIONS								SOURCES OF INFECTION FOUND				SIZE OF REACTIONS	
										FATHERS			MOTHERS			TOTAL FATHERS AND MOTHERS EXAMINED							
	NUMBER OF INFANTS UNDER 2 YR.	NUMBER OF CHILDREN	TOTAL	NEGATIVE	ACTIVE PRIMARY LESION	CALCIFICATION	PULMONARY REINFECTION	TOTAL NUMBER OF POSITIVE CASES	PERCENTAGE OF POSITIVE CASES	NUMBER	PERCENTAGE	PULMONARY TBC. FOUND	NUMBER	PERCENTAGE	PULMONARY TBC. FOUND	NUMBER	PERCENTAGE	PARENTS	OUTSIDE OF FAMILY	TOTAL NUMBER FOUND	PERCENTAGE	PERCENTAGE OF SMALL REACTIONS (1 OR 2 PLUS)	PERCENTAGE OF LARGE REACTIONS (3 OR 4 PLUS)
Sept., 1931 to Sept., 1937	18	146	164	151	6	6	1	13	7.9	38	23.1	0	54	32.9	2	92	28.0	2	28	30	18.2	82.0	18.0
Sept., 1937 to Sept., 1938	1	8	9	5	1	3	0	4	44.4	3	33.3	1	5	55.5	1	8	44.4	2	2	4	44.5	88.0	12.0
Sept., 1938 to Sept., 1939	3	27	30	26	3	1	0	4	13.3	20	66.6	0	24	80.0	1	44	73.3	1	11	12	40.0	60.0	40.0
Total	22 (10.8%)	181	203	182	10	10	1	21	10.3	61	30.1	1	83	41.1	4	144	35.6	5	41	46	22.6	76.7	23.3

izations whose function it is to examine the contacts of only known cases are at times unsuccessful due to the reticence still found among some people as regards acknowledging the existence of tuberculosis in their families. Organizations doing routine Mantoux testing, as in the case of the East Harlem Nursing and Health Service, often discover contacts to these patients known to the families, but not reported. This can be attributed to the fact that parents will not, as a rule, conceal the source of infection when made to realize that their children's health is at stake.

In the preparation of this material the data were collected in the three periods shown in Table III (September, 1931, to September, 1937, September, 1937, to September 1938, and September, 1938, to September, 1939). This was done because it was at first intended to prepare a report in September, 1937. This was not possible at that time. Since then the data of the two succeeding years have been added and are presented in the table in separate divisions because they bring out two interesting points. First, recent years show a greater willingness on the part of the parents to be examined; and, second, efforts to discover sources of infection are proving more successful.

A study of the size of the Mantoux reactions reveals that there is no correlation between it and the x-ray findings, nor is there any between it and the sex of the child. Referring to Table III, it can be seen that the size of the majority of the reactions to 0.1 mg. tuberculin was small, being either one plus or two plus. This is in accordance with the study conducted at Bellevue Hospital[1] which revealed that small reactions predominate over strong reactions in the first five years of life. The employment of this dosage of tuberculin as a routine, therefore, seems safe in this age group in the absence of a history of intimate exposure.

SUMMARY

The system of employing the Mantoux test routinely on supposedly noncontact infants and preschool children of a fairly large health center in New York City has proved advantageous to the community in the following ways:

1. During an eight-year period, 348 cases of tuberculous infection were found which would otherwise have gone undiscovered if reliance had been placed solely upon history of exposure or symptoms and physical examinations.

2. One hundred and twelve of these 348 cases were found within one year from the onset of the infection as a result of annually retesting previously negative Mantoux reactors. Early discovery meant early investigation of the source of infection, thus lessening the hazards from repeated and prolonged exposure.

3. The clinic is caring for 203 of these 348 children. The following findings are based on a study of these 203 cases.

4. One hundred and forty-four parents (35.6 per cent) were examined. Only five of these were found to have pulmonary tuberculosis.

5. Forty-six sources of infection were discovered. All but five were adults outside the immediate family. Fifteen of these persons were unknown as cases of pulmonary tuberculosis prior to our investigation.

6. The incidence of positive x-rays was 10.3 per cent. This relatively low figure is consistent with the existence of the source of infection outside the home in the majority of these cases, thus resulting in a smaller dosage of tubercle bacilli.

7. Treatment of these children included removal from the source of infection, adequate diet and rest, prevention of respiratory and contagious diseases, and preventorium and sanatorium care when indicated.

8. The educational value of the program is attested to by the increased knowledge of tuberculosis on the part of the medical and nursing staffs, and by the improved cooperation on the part of the parents. Most gratifying has been the ease with which the routine use of the Mantoux test has been accepted by the families under supervision of the East Harlem Nursing and Health Service. The district is taking tuberculosis in its stride, along with the knowledge of and efforts to eradicate diphtheria, smallpox, and other diseases.

CONCLUSIONS

This study is being conducted in a noncontact group which is not covered by the Department of Health. It includes primarily the infant and preschool ages in whom tuberculous infection has more serious immediate potentialities. The discovery of adult cases as sources of infection to these young children is an essential part of the work, and with improvement in our facilities for reaching the families, the number of such adults found continues to increase. The treatment of these children with primary infection is receiving particular attention, with a view of offering additional data on the much disputed point of the need for such treatment.

The ultimate aim of this study, however, is to carry the supervision of these children through and beyond the adolescent years in order to discover pulmonary tuberculosis as early as possible. The personnel and set-up of an organization, such as the East Harlem Nursing and Health Service make for the best type of relationship between the community and the health center. The years to come will show whether this relationship, combined with periodic x-ray examinations, will result in the discovery of a higher percentage of early pulmonary lesions. Whether such a program is practicable and valuable on a larger scale may not be learned for several years, but it is hoped that this report will encourage the present tendency to use the Mantoux

test routinely, at least in relatively small groups comprising infants and young children.

We wish to express our gratitude to Dr. Herbert R. Edwards, Director of the Bureau of Tuberculosis, Department of Health, City of New York, for generously placing the x-ray facilities of the Department of Health at our disposal, and to Miss Frances Boyle, clinic supervisor of the East Harlem Nursing and Health Service, for her valuable assistance in collecting the statistical data.

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ICTERUS GRAVIS NEONATORUM

End Results of the Syndrome of Nuclear Jaundice

Irwin Philip Sobel, M.D., and Joseph M. Zucker, M.D.*
New York, N. Y.

ONE of the dreaded complications of familial icterus gravis neonatorum is the so-called syndrome of nuclear jaundice (kernicterus). For many years clinicians have known that this syndrome is frequently accompanied by the death of the infant during the first two weeks of life. It now appears that the infant who lives through an attack of severe neonatal jaundice may be left with a neuromuscular dysfunction which makes a neonatal fatality seem a relatively fortunate occurrence. The earlier detection of cases of icterus gravis and the prompt application of modern methods of treatment may result in the saving of many lives which formerly would have been lost. Successful therapy may thus bring about the survival of patients without preventing the development of the syndrome of nuclear jaundice. The clinical picture of this syndrome is of interest since, with the recovery of a greater number of newborn infants from icterus gravis, there will appear a greater number of patients with impaired development demanding correct diagnosis.

Klingman and Carlson[1] found that, among 675 children with neuromuscular dysfunction characterized by choreoathetosis, ataxia, spasticity, and mental retardation, forty-five had passed through a severe neonatal jaundice, averaging ten weeks in duration. It is probable that most of these forty-five children represented the late stages in the syndrome of nuclear jaundice following icterus gravis.

Few post-mortem studies have been made upon patients who have survived the genuine syndrome of nuclear jaundice long enough for sequelae to develop. De Lange's patient[2] died at the age of 2 months. Following a neonatal episode of icterus gravis, the baby displayed extrapyramidal spasticity, a peculiar plastic opisthotonos, and athetoid movements. The anatomic findings consisted of a marked loss of ganglion cells in the globus pallidus and corpus subthalamicum (corpus Luysi) on both sides, together with a considerably increased gliosis and a marked demyelinization in the same regions.

Biemond and van Creveld[3] reported two infants with nuclear icterus concurrent with neonatal sepsis. Both patients died of bronchopneumonia at the ages of 3 and 4 months, respectively; both had had an umbilical infection during the first week of life; neither showed an erythroblastosis. These are the only cases of nuclear jaundice in the

From the Dr. Abraham Jacobi Division for Children, Lenox Hill Hospital, Service of Dr. Jerome S. Leopold, and the Neuropathological Laboratory of the Mount Sinai Hospital.

*Klingenstein Fellow in Neuropathology, Mount Sinai Hospital.

literature which did not follow icterus gravis. Septicemia was not proved by blood culture, and it may be that theirs was a genuine icterus gravis with an incidental umbilical infection. Both infants had shown extrapyramidal hypertonicity and marked opisthotonos. At necropsy the findings were essentially the same in each case. In the globus pallidus (especially in its internal portion) and the corpus subthalamicum there was extensive demyelinization, few myelin sheaths having been found. The same regions showed a great loss of nerve cells, but this was less intense than the degree of demyelinization. There was also a moderate degree of gliosis. No evidence of inflammation was present, nor was there an abnormal amount of fat or pigment. The substantia nigra was normal. There was a definite hypoplasia of the corpus callosum and of the anterior fornices in contrast with the size of the same structures in the normal brain of a child of about the same age.

Burghard and Schleussing[4] reported the case of a girl who, following icterus gravis (without anemia), developed convulsions, hypertonia, and opisthotonos. An eye ground examination revealed bilateral optic atrophy; an encephalogram demonstrated a moderate degree of internal hydrocephalus. The patient died at the age of 5 months. Bilaterally, in the globus pallidus, the corpus subthalamicum, the cornu ammonis, and the fascia dentata, the ganglion cells showed all degrees of marked damage, including complete disappearance. Fat was found both in ganglion cells and in macrophages. The destructive process was limited to the basal ganglia. A moderate glial response was present. Stains for myelin were not reported and apparently were not done.

Cornelia de Lange[5] reported the case of an infant who survived a moderately severe attack of neonatal icterus gravis but died of bronchopneumonia at the age of 6 months. The patient had been mentally retarded and had exhibited definite opisthotonos. At the time of the last admission to a hospital, a few days before death, the case was incorrectly diagnosed by an attending physician as being a meningitis because of stiffness of the neck (actually part of the peculiar opisthotonos associated with nuclear jaundice) and the temperature elevation (due to the pneumonia). The post-mortem examination disclosed a poverty of ganglion cells in the nucleus caudatus, the globus pallidus, and the putamen, with moderate gliosis. Grossly, the lamellations of the globus pallidus had been poorly demarcated. The substantia nigra seemed to be intact. In contrast to the brain of a normal newborn child, in which Weigert-Pal stains showed a denser myelin content in the globus pallidus than in the putamen, in this case the globus pallidus and putamen both showed a diminished, and more or less equal, myelin content. Swelling of myelin sheaths was seen and was assumed to be further evidence of myelin degeneration. In the

corpus subthalamicum, also, there was a lack of myelin substance, and the gliosis was more apparent. No fat or macrophages could be demonstrated. No changes were found in the medulla oblongata.

Zimmerman,[6] among a variety of cases, reported one case of an infant who, following an attack of neonatal icterus, developed spasticity of the extremities and retraction of the head, had convulsions, and showed mental retardation. The patient died at the age of 11 months. Necropsy revealed the patchy disappearance of many ganglion cells in the caudate nuclei, putamina, dentate nuclei, inferior olives, and cerebral cortex. The author accordingly assumed that the infant had had jaundiced basal ganglia during the episode of icterus gravis. However, the main purpose of his whole article had been to stress the changes in the nerve cells of the cerebral cortex, basal ganglia, and cerebellar cortex in infants and children due to a period of anoxemia resulting from convulsions before death in a variety of conditions.

Zimmerman and Yannet[7] made a complete pathologic study of the brain of a child who died three years after a severe attack of neonatal icterus gravis and nuclear jaundice. The manifestations of extensive cerebral dysfunction presented by the patient consisted of bilateral athetosis, generalized extrapyramidal muscular spasticity, mental retardation, and moderate opisthotonos and convulsions. At necropsy, extensive damage to the brain was described. The posterior horns of both lateral ventricles were strikingly dilated "as the result of shrinkage of the surrounding white matter which was soft and necrotic." Kulschitsky preparations for myelin demonstrated "the destruction of myelin sheaths. The process seemed to be old since but few phagocytes were present in the zones of softening." The optic nerves showed patches of demyelinization and slight amounts of fat. Far advanced degeneration of the lateral fibers of the spinal cord was found, especially in the region of the rubrospinal tracts. Again, very little fat could be found. The nerve cells were completely destroyed in the fascia dentata and the end plate of the lamina parietalis of the cornu ammonis. This was explained as due to necrobiosis although there was no softening of tissue in these regions and no proliferation of glia. A lack of large cells was noted in the corpus striatum. The number of small cells appeared to be normal in both the caudate nucleus and the putamen. The globus pallidus was described as being completely devoid of all nerve cells. In addition, it also lacked myelin substance. There were necrobiotic changes in the lateral thalamic nuclei. The corpus subthalamicum was almost invisible. The substantia nigra, grossly, had appeared to be absent. Microscopically its site was marked by a few nerve cells. There was also a paucity of nerve cells in the red nucleus. In the cerebral hemispheres, the nerve cells showed no evidence of necrobiosis, and the subcortex showed no degenerative changes.

The general post-mortem examination had disclosed one partially organized thrombus in the inferior vena cava involving the veins of the right kidney and right adrenal gland. Another such thrombus was found almost occluding the superior longitudinal sinus of the brain. There was no evidence of inflammation about these thromboses, and they were assumed to be a result of the patient's inanition. The authors repeatedly emphasized the "surprising finding" of marked degeneration of medullated nerve fibers and loss of nerve cells with no vestige of phagocytosis, no parenchymal softening, and no proliferative changes on the part of the glia.

The case of a 13-month-old child was reported by Bushnell and Aldrich.[8] At necropsy, the brain showed no evidence of nuclear jaundice, but there was an acute nonpurulent meningitis. De Lange[9] did not consider the case as clinically characteristic of nuclear jaundice and doubted the accuracy of the neuropathologic studies. She was of the opinion that no microscopic sections had been prepared and commented on the failure to report the staining techniques used. She believed that demyelinization might have been unobserved grossly because it was slight.

There are nine cases in the literature[10-16] which, although lacking post-mortem reports, may, on purely clinical grounds, be justifiably regarded as late cases of the syndrome of nuclear jaundice. All of these patients presented at least three of the following four signs: opisthotonos, mental deficiency, choreoathetoid movements, and extrapyramidal spasticity. In only three cases (the first case of Spiller, the third case of Zimmerman and Yannet, and the case of Illingworth) was opisthotonos not described.

Illingworth's case, a girl 11½ years old, is of especial interest since she is the oldest surviving patient recorded in the literature. Following icterus gravis in her first month of life, she displayed spasticity and choreoathetosis. Her physical and mental development was markedly retarded. At first she had appeared to be blind, and she did not try to help herself until her third year. She learned to walk at the age of 9 years. At 11½ years of age she still could not talk. She exhibited a marked generalized athetosis and frequent facial grimacing. Her limbs were spastic; knee jerks were present; a right Babinski sign was obtainable. A levulose tolerance test was reported as showing a gross defect of hepatic function.

There are two additional cases, without post-mortem study, in which the clinical basis for the diagnosis of nuclear jaundice is not sound. The patient of Greenwald and Messer,[17] aged 2 years and 4 months, displayed bilateral spastic diplegia, bilateral Babinski signs, and no superficial reflexes. Both physical development and the ability to speak were retarded. Cerebral symptoms had set in eleven months

after the neonatal episode of jaundice. The possibility of cerebral hemorrhage could not be entirely ruled out clinically. Two siblings had previously died of neonatal jaundice.

Guthrie's patient,[18] aged 1 year and 7 months, exhibited choreiform movements and mental deficiency, but no spasticity or opisthotonos.

The following case is that of a girl who, having passed through an attack of icterus gravis neonatorum seemingly complicated by the syndrome of nuclear jaundice, died at the age of 3½ years. She is the oldest patient in the literature of nuclear jaundice to come to autopsy.

CASE REPORT

History.—The patient was born on Dec. 17, 1934, when the mother was showing signs of a beginning toxemia. The infant was full term, and labor and delivery were normal. Jaundice appeared on the first day and increased daily thereafter. Three weeks after birth, the jaundice suddenly became much more marked and then gradually diminished over the course of another three weeks. Erythroblastosis and anemia were initially present. This portion of the patient's illness has been described in detail elsewhere.[19]

Following her recovery from the icterus gravis, she was subsequently examined in the outpatient department on three occasions: May 2, 1935, Aug. 1, 1935, and May 3, 1936, when she was, respectively, 4½, 7½, and 16½ months of age. During the first of these examinations it was observed that the child tended to lie on her right side and that the cranium was flattened in the right occipital region. The anterior fontanel measured 1½ inches in diameter. The patient would maintain a position of opisthotonos with the spine and head hyperextended. Her head could be brought forward against some resistance and, on release, reverted to its previous position. As she grew older, the opisthotonos increased, and spasticity appeared in the lower extremities. Then generalized spasticity developed, and during waking hours she began to exhibit purposeless squirming movements of the upper and lower limbs.

Her general development had been retarded. At the age of 1½ years she had only four teeth. She was forced to subsist on mashed foods. Vomiting was frequent, and she was incontinent of urine and feces. Antirachitic therapy had never been administered. The child was admitted to the hospital on May 16, 1938, at the age of 3 years and 5 months.

Examination.—Temperature was 99° F.; pulse, 120 per minute; respirations, 24 per minute; weight, 25 pounds; and height, 36 inches.

The patient had never been able to sit up, hold up her head, use her hands, or speak; she presented a picture of idiocy. She lay on her side with her head and spine in hyperextension and her thighs and legs flexed so that in side view her body presented the form of a question mark. Her head was acrocephalic with prominent frontal bosses and flattening in the right occipital region. It measured 20¼ inches in circumference. Her eyes did not follow moving objects. However, the eyelids would close when a bright light was flashed before them. The fundi were normal. The face was expressionless. There was a moderate rigidity of the neck, but, unlike that of meningitis, it was of a peculiar plastic sort and, as passive flexion was diminished, the head would return to hyperextension. The muscles of the trunk and the upper and lower extremities were markedly spastic. The upper and lower limbs displayed active choreoathetoid movements. The deep and superficial reflexes were normally active and equal. No pathologic reflexes were obtained.

The teeth were small, soft, and decayed, with the upper central incisors broken off close to the gingival margin. The anterior chest wall presented a rachitic rosary, Harrison's grooves, and a funnel-shaped depression in the sternum. The heart and lungs were negative. Manual examination of the abdomen was negative, neither the liver nor the spleen being enlarged. The remainder of the physical examination was likewise negative.

Laboratory Data.—The urine showed a trace of albumin. Blood microscopy showed hemoglobin, 12.0 Gm. per cent (Sahli); erythrocytes, 4,310,000 per c.mm.; leucocytes, 10,000; differential, polymorphonuclear neutrophiles, 50 per cent (of which 40 per cent were immature forms); lymphocytes, 47 per cent; monocytes, 3 per cent. Blood chemistry showed serum calcium, 11.1 mg. per cent; serum phosphorus, 5.0 mg. per cent. Roentgenographically the skull revealed thinning of the bony tables and some increase of the convolutional markings.

Course.—A roentgenogram of the lungs taken on the afternoon of admission disclosed an area of dense consolidation in the right upper lobe. The following day dullness appeared over the right chest anteriorly, and crepitant râles were heard. The temperature rose steadily to 107.4° F., and the patient died on May 18, 1938, about thirty-six hours after admission.

NECROPSY FINDINGS

General.—The child's body was emaciated. In the upper lobe of the right lung there was a firm purple area of bronchopneumonia. The heart, aorta, spleen, gall bladder, pancreas, gastrointestinal tract proper, kidneys, and genitals showed no significant pathologic changes. The liver was reported as showing congestion and fibrosis in the portal areas. The walls of its larger arteries were described as being thickened.

Brain. Gross Examination.—The brain was well developed and symmetrical. The superficial blood vessels were engorged, and the cerebral convolutions were swollen. The vessels of the base were normal. No thrombi were found in any of the blood vessels, and there was no evidence of old or recent cerebral hemorrhage. The optic nerves and chiasm were soft and edematous. On sectioning the brain, the ventricles were found to be moderately dilated. There was no gross evidence of changes in the cerebral hemispheres, basal ganglia, cerebellum, brain stem, or choroid plexus.

*Microscopic Examination.**—Throughout the cerebral cortex and subcortex, the corpus callosum, and the nuclei and tracts of the diencephalon, there were small, discrete, irregularly shaped areas of rarefaction (Fig. 1). They were more conspicuous in the cerebral subcortex, the corpus callosum, and the diencephalic tracts than in the cerebral cortex and diencephalic nuclei. They were present in the optic tracts but not in the optic nerves. In the putamen and thalamus they were more prominent than in the globus pallidus. The globus pallidus stained more lightly for myelin than did the putamen (Fig. 2). The corpus subthalamicum showed a marked decrease in myelin-staining substance. A section of the medulla at the level of the lower end of the pyramidal decussation presented circumscribed oval areas, lacking myelin substance, in the region of the pyramidal tracts (Fig. 3).

In the cerebral subcortex, the corpus callosum, and the diencephalic tracts, the areas of rarefaction consisted of spaces unstained except for a few interlacing fibers

*The brain of this case was restudied about a year after the autopsy. Only the region of the red nucleus was not available.

The tissue was studied in paraffin, celloidin, and frozen section. Hematoxylin-eosin was used as a general cytoplasmic stain. Celloidin-imbedded material proved refractile to the Nissl (toluidine blue) stain, but fairly satisfactory Nissl preparations were obtained with paraffin and frozen sections. Myelin substance was stained by the Spellmeyer and Weil techniques. Scarlet Red (Sudan IV) was used to demonstrate fat. Glia were stained with the Globus modifications of the Hortega silver carbonate and Cajal gold sublimate techniques, as well as with the Mallory (Greenfield modification) phosphotungstic hematoxylin and Holzer stains.

and a few, small, round nuclei. Special stains showed that these nuclei were usually oligodendroglial. In the cerebral cortex and diencephalic nuclei the areas of rarefaction were lightly-staining patches which contained no fibers and frequently only a single oligodendroglia or none at all. Occasionally the areas of rarefaction were found in series along the course of blood vessels. They were free of fat particles, and only on one occasion was an accumulation of fat found about a neighboring, fairly large blood vessel.

Fig. 1.—Photomicrograph showing the small diffuse areas of rarefaction in the cerebral cortex and subcortex, frontal lobe. (Mallory phosphotungstic hematoxylin, Greenfield modification, ×50.)

Fig. 2.—Photograph of a transverse section through the diencephalon, showing the lenticular nucleus on one side and the subthalamus on the other. The globus pallidus shows a lack of myelin substance in contrast to the putamen. The pallor of the corpus subthalamicum was more marked in the original section than it is in the photograph. The small areas of rarefaction are seen everywhere in the more deeply-staining regions of the section. (Weil myelin stain, ×2½.)

Fat droplets rarely occurred free in the brain tissue proper and not much more often in phagocytes. In the cerebral cortex many capillaries were completely enveloped by fatty substance. In the cerebral subcortex, perivascular accumulations of fat were fewer and were found about larger vessels. Perivascular aggregates of fat droplets were also seen in the diencephalon but less often than

in the cerebrum; and the globus pallidus showed less fat than the head of the caudate nucleus and adjacent internal capsule. One large vessel in the thalamus disclosed fat in the medial coat. No fat was found in the corpus callosum, the midbrain, or the medulla.

In the cerebral cortex the cellular architecture frequently seemed to be disturbed, and there was a decrease in the number of nerve cells, especially in the third and fourth layers. The nerve cells in the cerebral cortex were usually swollen; some were sclerotic. Of the swollen cells, some exhibited an irregular, vaguely defined cell outline; their cytoplasm was finely granular and stained poorly, if at all; and the nuclei, staining homogeneously, were located in the implantation cone of the axon. Somewhat similar changes were found in the nerve cells of the diencephalon. In the globus pallidus and corpus subthalamicum there was, also, a more apparent decrease in the number of nerve cells. In the dentate nucleus of the cerebellum most of the nerve cells were swollen; some showed vacuoles in their cytoplasm, vagueness of outline, and granular staining of the cytoplasm. The cells of the substantia nigra were well preserved. In the medulla, the nerve cells showed swelling with some loss of cellular detail.

Fig. 3.—Photograph of a section of the medulla at the lower level of the pyramidal decussation, showing clearly the largest of the areas lacking myelin in the pyramidal tracts. (Weil myelin stain, ×12.)

In the cerebral hemispheres and diencephalon there was a diffuse increase in glia. Many of these were oligodendroglia, frequently occurring in small groups. Most of the oligodendroglia were rounded; some were swollen; others showed process formation. Occasional astrocytes were seen which often showed swelling and clasmatodendrosis (Fig. 4). At times fibrillary astrocytes were also encountered. In the corpus callosum, astrocytes were more frequently met with but were not pathologically increased in number.

The leptomeninges in the parietal region were loosely thickened and were infiltrated with mononuclear cells. The ependymal lining of the fourth ventricle

was coated with a thin film of fibrinous material, occasionally containing a mononuclear cell.

Medium-sized blood vessels in the cerebral hemispheres and diencephalon occasionally showed masses of fibrin within their lumina. However, there were no signs of inflammation or necrosis in the tissue surrounding these vessels. Some of the smaller vessels showed thickened walls, and perivascular spaces were often enlarged.

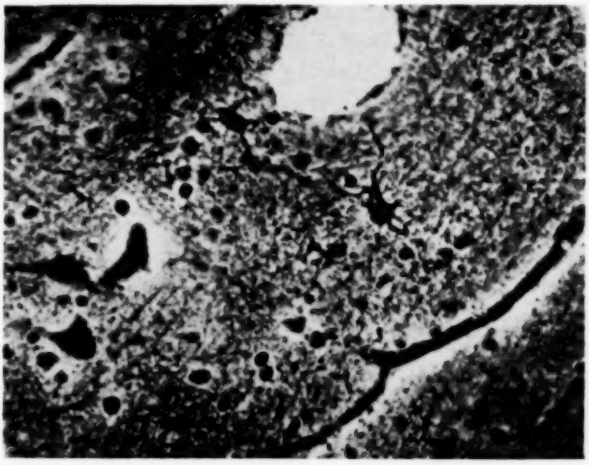

Fig. 4.—Photomicrograph from a section of the thalamus showing the nature of the gliosis—a diffuse increase in oligodendroglia and occasional swollen astrocytes with fragmented processes. (Hortega silver carbonate, Globus modification, ×580.)

Summary of the Pathologic Findings.—The essential pathologic changes consisted of diffuse alterations in the cerebral hemispheres and diencephalon. They were in the nature of nerve cell absence and degeneration, multiple small areas of rarefaction, a moderate degree of gliosis (chiefly oligodendroglial), and a moderate increase in perivascular fat accumulations with relatively few phagocytic cells. The nerve cell changes and the fat accumulations were more prominent in the cerebral cortex. Fat was not associated with the areas of rarefaction. The globus pallidus and the corpus subthalamicum showed a diminution in myelin content in addition to the relative decrease in the number of nerve cells. In the medulla at the level of the lower end of the pyramidal decussation there were a few oval areas, lacking myelin, in the region of the pyramidal tracts. In several cerebral and diencephalic blood vessels there were masses of fibrin. A nonpurulent meningitis and ependymitis were also present.

No definite conclusions can be drawn from these findings. Diffuse alterations were present, but whether these were specific or to be associated with the patient's prolonged malnutrition cannot be stated. The pathologic findings were not those of a system disease. The early stages of thrombosis in some of the blood vessels was apparently a terminal feature.

DISCUSSION

The patient, after recovering from a severe attack of icterus gravis neonatorum, began to display evidence of extensive brain damage. The following four cardinal signs, associated with the late syndrome of

nuclear jaundice, were present: (1) choreoathetosis; (2) extrapyramidal spasticity; (3) opisthotonos; and (4) mental deficiency. The child lived for three and one-half years with each of these signs becoming progressively more pronounced.

Although the patient presented the complete clinical picture of the end result of nuclear jaundice, necropsy did not reveal the positive findings necessary to substantiate this diagnosis. To claim justifiably from the pathologic examination that a patient had survived an attack of nuclear jaundice following icterus gravis neonatorum, two criteria must be met. In the first place, the lesions should be limited to the striatopallidal portions of the brain which, during the acute phase of the disease in the typical instance, are stained with bile pigment and show evidence of cell destruction. In the second place, the late lesions observed must be of a kind which prove that a previous destruction of nerve elements in this system has taken place, as demonstrated by: (1) loss of nerve cells; (2) demyelinization; and (3) glial proliferation. Neither of these two criteria was satisfied in the present case which showed diffuse changes of moderate degree scattered throughout the cerebral hemispheres and the diencephalon.

The patient herein described presented in classical form the clinical picture of a late survivor of severe nuclear jaundice without, however, revealing the pathologic findings reported to be associated with this syndrome.

CONCLUSIONS

The case of a girl is reported who lived for three and one-half years following a severe attack of icterus gravis neonatorum and who demonstrated clinically the end results of the syndrome of nuclear jaundice.

The characteristic tetralogy presented by survivors of nuclear jaundice —choreoathetosis, extrapyramidal spasticity, opisthotonos, and mental deficiency—was prominent in this case.

Pathologic examination, however, did not disclose the findings in the central nervous system which have been reported in the literature as the underlying anatomic basis for this clinical syndrome.

We wish to express our sincere appreciation to Dr. Joseph H. Globus for his aid and guidance in the study of this case and in the preparation of this report.

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INFLUENZAL MENINGITIS

NELLES SILVERTHORNE, M.B. (TOR.), AND ALAN BROWN, M.D., WITH THE TECHNICAL ASSISTANCE OF W. M. JOHNSTONE AND AGNES WALKER
TORONTO, ONTARIO

THE treatment of influenzal meningitis by the use of serum and drugs, as well as other aspects of this perplexing disease, has been the subject of a number of publications[1-22] in recent years. The stimulation of an interest in the subject of therapy in influenzal meningitis is largely due to the investigations of Ward and Wright,[2] Fothergill and co-workers,[3-6, 9, 11] and Pittman.[7] Following the method recommended by Dr. Fothergill, Silverthorne, Fraser, and Snelling[14] published their results on the treatment of thirty-six patients with influenzal meningitis. Twenty-six of the patients died, a mortality of 72 per cent, which was a striking decrease over the past mortality of 98 per cent. The present communication is a progress report on the treatment of a larger number of patients and includes all of our results up to the time of writing. A small number of patients who have not received specific treatment has been excluded from the series. These were critically ill and, in most instances, died before treatment could be instituted. In addition to the results of therapy, bacteriologic and serologic investigations on meningeal strains of *Hemophilus influenzae* will be reported.

Clinical Data.—The treatment of sixty-five infants and children suffering from influenzal meningitis forms the basis of this study. If we examine the outcome of patients with this disease over a twenty-year period, it will be observed (Table I) that, from the histories of seventy

TABLE I

INFLUENZAL MENINGITIS

NUMBER OF PATIENTS	YEARS	TREATMENT	DEATHS	MORTALITY
70	1919-1929	Nonspecific	69	98%
65	1930-1939	C.I.,* transfusion, Specific sera, L.P.,† drugs	50	76%

*C.I., Continuous intravenous injection of glucose saline.
†L.P., Lumbar puncture (daily) and drainage.

patients during the years 1919 to 1929, there were sixty-nine deaths, a mortality of 98 per cent. During the next period from 1930 to 1939, sixty-five patients were treated as indicated in the table, and there were fifty deaths, a mortality of 76 per cent. It is thus obvious that

From the wards and laboratories of the Hospital for Sick Children and the Department of Paediatrics, University of Toronto, and the Connaught Laboratories, University of Toronto.

a significant reduction in mortality has occurred. In reviewing the histories for the most prominent symptoms, the reporting of a "head cold" occurring from two days to one month prior to the onset of meningeal signs was obtained in thirty-one of the sixty-five patients. Symptoms of fever, vomiting, drowsiness, and irritability were elicited in the majority of instances. In a moderately large number of patients, the parent reported the complaint of "soreness of neck" or "stiffness of neck" on attempted movement of the child. The age distribution is similar to that reported by Fothergill and Sweet[5] and by Silverthorne and co-workers,[14] in that 69 per cent of the patients were in the first three years of life. A summary of the various methods used in the treatment of the patients is given in Table II. It is to be

TABLE II

INFLUENZAL MENINGITIS

METHOD OF TREATMENT	NUMBER TREATED	DEATHS	MORTALITY
Human serum	1	0	
Anti-influenzal horse serum plus human serum	35	28	80%
Anti-influenzal horse serum plus human serum plus sulfanilamide or sulfapyridine	3	3	100%
Anti-influenzal horse serum plus bactericidal guinea pig serum	14	11	78%
Anti-influenzal horse serum plus bactericidal guinea pig serum plus sulfanilamide or sulfapyridine	10	7	70%
Immune anti-influenzal rabbit serum plus sulfapyridine	1	0	
Sulfapyridine (moribund)	1	1	100%

observed that there is little difference in the mortality between those patients treated by Fothergill's method (anti-influenzal horse serum intravenously and anti-influenzal horse serum and human serum [complement] intrathecally) and those treated with anti-influenzal horse serum intravenously and bactericidal guinea pig serum intrathecally. In a previous article,[14] the author referred to the method of producing bactericidal guinea pig serum. Since there is little difference in mortality as a result of the use of Fothergill's method of treatment or the use of guinea pig serum in treatment, we propose to discontinue the production and use of the latter serum. It may be mentioned, however, that one year we had three consecutive recoveries after using immune bactericidal guinea pig serum intrathecally. The necessity of repeatedly injecting and testing large numbers of guinea pigs to obtain small amounts of immune serum for use in treatment renders this method impractical. At present we have been interested in the development of an immune rabbit serum which shall be referred to in more detail later.

Bacteriologic Investigations.—During the past four years we have made a study of thirty-two cerebrospinal-fluid strains of *H. influenzae*

from our patients. Experimental observations of the following nature have been made (Table III): appearance of the gram-negative bacilli

TABLE III

BACTERIOLOGIC DATA

STRAINS	MORPHOLOGY	COLONIAL APPEARANCE	ODOR	SATELLITE GROWTH	INDOL PRODUCTION	HEMOLYSIS	AGGLUTINATION WITH IMMUNE HORSE SERUM	TYPE	VIRULENCE 10^{-3}-10^{-8}
32	Pleomorphic	Typical smooth	Characteristic	+	+*	-	+	B†	+‡

*One strain did not produce indol.
†One strain did not type in A, B, C, D, E, or F serum.
‡Four strains did not show mouse-mucin virulence.

in the smear from spinal fluid, colonial characteristics on blood agar heated to 80° C. for fifteen minutes, odor, satellite growth around *Staphylococcus aureus*, growth on plain agar, indol production, hemolysis on blood agar, utilization of carbohydrates, agglutination in normal and immune horse serum, type, and virulence. The microscopic appearance of the gram-negative bacilli is quite characteristic when examined directly from spinal fluid. The bacilli vary from short rods to longer bacillary forms and usually occur in fairly large numbers. After early subcultures they are more uniform in size and appear much shorter in length. The colonial appearance of freshly isolated strains, grown on blood agar heated to 80° C. for fifteen minutes, is uniform. The colonies reflect light, are smooth in outline, and do not show indentation of their borders. In other words, they are typical smooth colonies. There is also a fairly characteristic odor of the growth on blood agar (80° C. for fifteen minutes). None of the strains isolated grew on plain beef infusion agar. All strains, with the exception of one, produced indol. None of the strains produced hemolysis on blood agar. Carbohydrate reactions revealed that all strains utilized dextrose and not saccharose. Our results with maltose have been variable. The strains have been typed according to the method of Dr. Margaret Pittman.[1] Thirty-one of thirty-two strains examined fall clearly into Type B grouping. Virulence tests were done by injecting suspensions of freshly isolated strains with mucin into mice. A technique was used similar to that reported by Rake[23] in his work on the meningococcus. Twenty-eight of the thirty-two strains were found to have some degree of virulence, varying from 10^{-3} to 10^{-8}. Four strains showed no virulence in mice. It is quite evident from these findings that cerebrospinal-fluid strains from cases of influenzal meningitis are, in the main, a homogenous series, with a few minor exceptions. These exceptions are as follows: one strain did not

produce indol; one strain was not Type B; and four strains did not possess virulence when injected with mucin intraperitoneally into mice.

IMMUNE SERUM

It will be observed from Table I that one patient, who was treated recently with sulfapyridine and immune rabbit serum, recovered. We have shown that most of our patients have been treated with various serum mixtures and that, before the use of chemotherapeutic agents, we had reduced our mortality in cases receiving serum. Our results with sulfanilamide and sulfapyridine are so far not convincing enough to recommend the use of drugs alone. Due to the many technical difficulties in the production of guinea pig serum and with the knowledge of the beneficial effect of rabbit serum containing mouse-protecting antibodies in the treatment of other infections, we have developed an immune anti-influenzal rabbit serum which contains mouse-protecting antibodies against a fatal infection with meningeal strains of *H. influenzae*. This serum we have used, along with sulfapyridine in one case, with gratifying results. In the future we propose to treat some of our patients with this combined therapy. The following is a description of the mouse protection test we have used in testing the immune bodies developed in rabbits injected with freshly isolated *H. influenzae*. The method of injecting rabbits has been reported by Pittman. In addition, we have injected the rabbits with 1 c.c. daily for one week, with a rest period of one month, followed by a similar series of daily doses for one week with a rest period of one month, and then another similar course of injections. Following these injections, rabbit serum was found to contain mouse-protecting antibodies.

Technique of Mouse Protection Test.—Young white Swiss mice are used. One-half cubic centimeter of normal and immune rabbit serum is injected intravenously into the tail vein of each of three mice, for each dilution of serum (e.g., 1:2, 1:5, 1:10, and 1:50 dilutions). Three hours later 1 c.c. of a suspension of a freshly isolated strain of *H. influenzae* suspended in mucin in a 10^{-2} dilution (from a six- to eight-hour growth and a standard suspension of Gates 4 turbidometer density) is injected into each mouse receiving normal rabbit serum and immune rabbit serum. At the same time, mice which have not received serum are injected with the same mucin bacterial suspension as a control of the virulence of the culture in mice.

Results.—In a series of experiments we have found that, with this technique, mouse-protecting antibodies are developed in the serum of rabbits injected (as described) with meningeal strains of *H. influenzae*.

DISCUSSION

Although from a perusal of Tables I and II it is evident that the mortality of influenzal meningitis has been reduced, we believe that a

combination of the therapeutic procedures used in treatment rather than any individual factor is responsible for the reduction in mortality. It is obvious that recoveries have occurred with Fothergill's method, also with guinea pig bactericidal serum containing complement and with sulfapyridine and immune rabbit serum containing mouse-protecting antibodies. Certain patients, and especially infants, still die of this disease, and in the latter cases the mechanical difficulties of removing inflammatory exudate which is intimately adherent to brain tissue are most likely the cause of our failures. The prognosis is extremely poor in patients who begin to "twitch" or "convulse" early in the course of treatment. In our experience we do not recall a patient recovering who convulsed repeatedly during the course of the disease. It will be remembered that four strains isolated from our patients were not virulent in the mouse-mucin test. Three patients who harbored three of these avirulent strains recovered. This fact may be another reason why some patients respond to treatment.

From a bacteriologic standpoint the most noticeable feature is the relative homogeneity of the strains isolated. With few exceptions, they have reacted identically both biologically and culturally.

In discussing the future of treatment, we believe that the use of a chemotherapeutic agent, combined with Fothergill's method of serum therapy or immune rabbit serum, is worthy of continued trial. In addition, we are convinced that adequate amounts of intravenous fluids and daily lumbar puncture with drainage will further the chances of recovery in each patient.

SUMMARY AND CONCLUSIONS

Intensive treatment of influenzal meningitis has reduced the mortality in this disease.

Bacteriologically, meningeal strains of *H. influenzae* form a homogenous series with few exceptions.

The use of chemotherapeutic agents with immune serum mixtures is to be recommended rather than the use of either drug or serum alone. In addition, continuous intravenous therapy and daily lumbar puncture with drainage should be carried out.

A mouse protection test for measuring immune bodies in serum obtained from rabbits receiving injections of freshly isolated strains of *H. influenzae* is reported.

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THE MECHANICAL RESPIRATOR IN POLIOMYELITIS

JAMES L. WILSON, M.D.
DETROIT, MICH.

OVER ten years ago a mechanical respirator was first used on a child with infantile paralysis. Since then the respirator has been greatly improved and has attained notoriety under the name "iron lung." The general impression is held that most patients put in the machine die; or that, if they survive, they are hopeless cripples. This impression exists because of a misconception of one of the important purposes of the respirator and because of injudicious selection of patients. Regardless of reported results, the respirator as used in the treatment of poliomyelitis is here to stay. Public opinion alone demands that every attempt possible be made to prolong life.

The present paper will make no attempt to evaluate the respirator statistically. What we really need to know is not how many patients died despite this treatment, nor how many lived who would have died without it, but how much improvement there is in the respiratory muscles of the patients who received early and adequate rest through its aid. The writer believes, first, that there is still a great confusion about the selection of patients for treatment, and, second, that a misconception exists as to what should be the purpose of respirator treatment.

Despite the obvious fact, it needs to be stated again that the respirator will aid only when there is paralysis of the intercostal muscles or diaphragm, or in the rare instances where there is a hypofunction, not a dysfunction, of the respiratory centers. It will not help when pharyngeal paralysis obstructs respiration, when the respiratory centers are irregularly active and produce something like an auricular fibrillation of respiration, or when respiratory failure is secondary to circulatory collapse and tachycardia, as is so frequently the case in this disease. It will not help, therefore, in most cases of "bulbar" poliomyelitis, except where the paralysis of muscles innervated from the medulla is complicated by intercostal or diaphragmatic paralysis. The bulbar cases outnumber the cases of peripheral respiratory muscle paralysis in any epidemic; so it is not surprising that physicians who place in a respirator every patient with respiratory symptoms, regardless of their nature, have only an unhappy experience with a series of patients with "bulbar" poliomyelitis futilely treated.

From the Department of Pediatrics, Wayne University, and the Children's Hospital of Michigan.

Poliomyelitis can prevent efficient respiration in three ways:

1. By actual paralysis of the primary respiratory muscles, the intercostals and the diaphragm, due to damage to the anterior horn cells of the cord.

2. By disturbance of the nerve centers in the medulla or bulb which presumably control the rate, rhythm, and depth of respiration.

3. By the collection of mucus or vomitus around the glottis in patients with paralysis of the pharynx, causing constantly interrupted inspiratory efforts resulting in shallow, irregular, and ineffective respiration.

In the first situation, that with actual paralysis of the intercostal muscles or of the diaphragm, the lesion exists in the dorsal and cervical cord. This type, therefore, should not be classed as bulbar, although respiratory failure occurs.

The lesions existing in the second and third situations, involvement of the respiratory centers or paralysis of the pharynx, are in the medulla, and, therefore, this type is commonly and properly called bulbar.

The respiratory difficulty in any patient ill with poliomyelitis may be due to a single one of these three factors or to any combination. Paralysis of the respiratory muscles very frequently occurs alone without bulbar complications. Paralysis of the pharynx, the palate, or the facial muscles, all innervated from the medulla, is very frequently associated with apparent involvement of the "vital centers," most evidently the respiratory center. The marvelously complicated and congested mass of nerve paths and nerve centers of the medulla makes it remarkable that such association does not always occur.

The therapeutic use of the Drinker respirator in poliomyelitis is most logical and has proved most effective, not in the bulbar forms of poliomyelitis, but in patients with paralysis of the intercostal muscles or of the diaphragm.

It is particularly unfortunate that most physicians, like most laymen, think of the respirator only as a machine for saving life and for aiding breathing until enough recovery takes place to enable the patient to carry on by himself. This is a regrettably limited point of view and ignores what is probably the most valuable function of the respirator. *The respirator should be considered as a device for providing physiologic rest for the muscles of respiration.* We have learned, on firm grounds of experience, that a paralyzed arm should be put at rest immediately when weakness is detected; so soon, in fact, that the more conservative of us do not even delay to measure fully the degree of paralysis before splinting the arm. With the respiratory muscles, however, the common attitude is unfortunately different. Many wait for signs of marked dyspnea, or even for the premortal sign of cyanosis, before attempting to rest the respiratory muscles. This delay is ex-

plained partly by the difficulty of detecting the early signs of paralysis of the respiratory muscles, partly by the difficulty of obtaining a respirator, and, worst of all, by the dread of initiating its use. The result of all this is that the respiratory muscles are allowed to suffer a degree of fatigue which would be considered a sign of intolerable neglect, were the muscles those of the arm; and it explains the unsatisfactory outcome of respirator treatment of a good many cases. There are many patients who survive poliomyelitis without benefit of respirator who might have better respiratory muscles today if they had had that treatment.

The early evidences of paralysis of the intercostal muscles or the diaphragm may be difficult to recognize and to interpret. Wakefulness, anxiety, restlessness, an increase in respiratory rate, the dilatation of the nostrils, a slight respiratory grunt, disinclination to talk, or a curious, frequently interrupted, monosyllabic speech—all may precede more marked evidences of paralysis. Occasionally a slow, irregular, shallow respiration surprisingly conceals a respiratory weakness. None of these signs are, of course, specifically indicative of paralysis of the muscles of respiration, but they demand very careful examination.

In a child who will not cooperate by "taking a deep breath" it may be helpful in the demonstration of a partial paralysis of the muscles of respiration to inhibit the action, first, of the intercostals, and then of the diaphragm, by splinting the chest or the abdomen with the hands and thus forcing the alternate respiratory muscles to greater action. Paralysis of both shoulders is so frequently associated with paralysis of the intercostal muscles that, when this is detected in the acute stage of the disease where further extension might occur, the respiratory muscles should be carefully watched. With any evidence of respiratory weakness or with paralysis of both shoulders in the acute stage of the disease, every effort should be made to move the patient to a respirator. Paralysis may extend with such rapidity that an hour or two may change a situation in which careful and deliberate arrangements can be made to one which necessitates desperate speed with frequently resulting harm and distress to the patient.

In the individual patient with bulbar poliomyelitis without paralysis of the intercostal muscles or of the diaphragm, it is often difficult to untangle the causes of the respiratory difficulty. In some cases the respiratory disturbance seems purely "central" in origin and may make itself manifest by shallow, irregular respirations or by jerky, spasmodic inspiratory efforts, sometimes almost amounting to a succession of hiccoughs. If the disturbance is purely central in origin and if the patient's own respiratory efforts are unsuccessful in properly ventilating the lungs, the respirator may justifiably be given a therapeutic trial. For the most part, however, such patients are little helped by the apparatus. Their own irregular, inefficient respiratory efforts

do not synchronize with the rhythm of the machine, but, rather, prevent its effective action.

Many patients are taken out of the machine too soon. Physicians thinking only of the immediate emergency take a patient out of a respirator as soon as he seems to be able to survive unaided. Not infrequently patients may return after a few days or a week at home with what is called an "exacerbation" of their paralysis, which is in reality only a result of accumulative fatigue. The reasons for this are obvious —the desire to get the patient home, his own wish to be in a bed, and, most of all, the expense of the respirator and the other demands for its use. Despite these things, however, it is most important that rest periods in a respirator should be continued for many days; in intercostal paralysis short intervals of artificial respiration should be a part of physiotherapy over long periods.

The construction of the Drinker respirator has changed considerably since its introduction, and it has been greatly improved. The usual "iron lung" seen in movies, and even at fairs, is now quiet, no longer needs a crew to open and close it, and has facilities permitting fairly good care of the patient inside. In addition, two new types have appeared which offer great possibilities.

A room-size respirator, caring for several patients at once, has been constructed and has given excellent results.[1] Experience has proved that it is perfectly satisfactory to apply a single rate of respiration and degree of pressure to all patients, even though they may differ widely in age. The great advantage of this form of respirator lies in the ease of carrying out the proper nursing and orthopedic care, for lack of which a good many patients have died in the standard machine. These patients are apt to develop hypostatic pneumonia, making it necessary to turn them at a time when their pain demands the most gentle handling, which is difficult in even the most modern of the individual machines. The greater ease of handling in this respirator room of course makes the nursing care cheaper as well as more satisfactory. The use of the room respirator has not spread for several reasons, such as the fear of its cost, which is exaggerated, and the space it occupies.

A third type of respirator is being developed. Several workers have given thought to it, and several variations on the basic design are being manufactured. Essentially, it consists of a rigid or semirigid cuirass or jacket made to be put on the chest and abdomen and making an airtight space over the body. The intermittent evacuation of this space by means of hand- or motor-driven pumps causes respiration to be induced by the same principle as in the Drinker respirator. Many details remain to be worked out. Some of the trial machines make an airtight connection along the sides of the body with the rubber sheet of the bed; others fit clear around the body. The most

quickly adjusted and simplest and the one the writer believes most promising makes its contact entirely on the body by a soft partially inflated rubber tube. It is not the purpose of this article to detail construction; it is sufficient to say that these small machines will have certain great advantages if they are kept simple, and that it is to be hoped that competitive manufacture will evolve the best and cheapest. These jacket respirators are light and portable, requiring little space for storing. They can be applied very quickly, some types almost instantly. They should be very inexpensive. Good nursing and orthopedic care are easily carried out during their use. They are comfortable and less frightening than the other types, but they have certain disadvantages. Several sizes will be necessary to fit a variety of patients; but this should not be serious, as the jackets are sufficiently flexible to allow four sizes to take care of all infants and children, and one power unit can be used interchangeably with all of them. It is probable that they will not expand the upper thorax unless they are made so complicated and cumbersome as to discount their other advantages. They will act primarily on the diaphragm, which is perfect physiologic procedure in the child, though less so in the adult; and possibly they will be less suitable for treatment of poliomyelitis over a period of many weeks since they will not aid in expanding the chest wall in a patient with an efficient diaphragm. A greater pressure change will be necessary than in the Drinker respirator.

The possibilities for use of these small respirators in emergency treatment of conditions other than poliomyelitis are very encouraging. The field of emergencies, including gas poisoning, electrocution, drowning, respiratory failure under anesthesia in crowded operating rooms, and cord injuries, is hardly covered by the Drinker respirator because of its immobility, size, and expense. If simplicity is not sacrificed, and, of course, if the machines are readily available, they can be made to act as quickly as the Schäfer method of artificial respiration and far more effectively and without trauma. They can act equally well with the patient prone or supine. They would seem to be the ideal mobile supplement to the room respirator during poliomyelitis epidemics, since, by the use of hand-operated jacket respirators, patients can easily be transported to the stationary multiple patient units.

It is easy to criticise the use to which the respirator has been put up to this time and to recommend its far more extensive utilization. However, if all patients in any epidemic of poliomyelitis were ideally cared for, a great many more machines would be necessary to carry the peak load. To do this, it would be necessary for many hospitals carrying on their work in epidemic areas to make their purchases and, we should hope, construct a room respirator far ahead of actual need and on a basis of an uncertainly predicted maximum require-

ment. Many times equipment would be bought which would never be needed.

It would seem greatly to be desired that the whole problem of the respirator in poliomyelitis be handled on a broad scale, so that the burden of local outbreaks could be spread over other communities, and so that an expensive machine, purchased by one hospital for an emergency and used once or twice, should not be immobilized there and allowed to collect dust unused, while other hospitals go belatedly through the same expensive procedure. If plans were made ahead, a knockdown room respirator could be constructed which might be erected in a few days at some central place in an epidemic area; and in the meantime, the single machines, either the "iron lung" or the new jacket respirator, could be made available as a supplementary unit, both for the less seriously paralyzed patients and for use in transport to the more ideal room respirator. It seems unlikely that, through private individual initiative and uncoordinated efforts of physicians and hospitals, enough good machines will ever be made available to give ideal care to all patients in any epidemic of poliomyelitis. A well-organized and controlled plan, making use of a mobile group of respirators of various types loaned by some central charity, seems the only way to meet the situation satisfactorily.

SUMMARY

The respirator in poliomyelitis should be used as a means of giving physiologic rest in early and moderate paralysis of the respiratory muscles. The dramatized use of the respirator as an emergency life-saving machine has occurred at the expense of interest in its more prosaic, but perhaps more valuable, function as a splint for weakened respiratory muscles.

The early signs of respiratory weakness are often undetected, and the patient is given either no respiratory treatment at all, or none until a degree of fatigue occurs which would be considered a sign of intolerable neglect, were the muscles those of the arms.

No clear distinction is made by many physicians between the various causes of respiratory failure in poliomyelitis. The respirator is seldom of use except where the intercostal muscles or diaphragm are paralyzed. Most cases of "bulbar" poliomyelitis are not helped.

Two new types of machines for artificial respiration are described and their different advantages discussed.

It is suggested that a national coordinated program for the handling of respiratory paralysis in poliomyelitis be planned as the only practical manner of meeting this problem.

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ROCKY MOUNTAIN SPOTTED FEVER IN CHILDREN

DAVID W. MARTIN, M.D.
DURHAM, N. C.

THERE has been little in pediatric literature on Rocky Mountain spotted fever in children, despite the fact that in the East, where the infection is transmitted by the common dog tick *(Dermacentor variabilis)*, children between the ages of 5 to 14[1] are the most frequent sufferers from the disease because of their play habits which make them more likely than adults to pick up ticks. It was not until nine years[2] ago that the disease was differentiated in the East from typhus fever and that cases were reported as Rocky Mountain spotted fever. Shipley[3] reported six cases in children from the files of the Johns Hopkins Hospital in 1932. Since that time the number of reported cases in most of the eastern and southern states has gradually increased. This apparent increase in cases reported is probably due to the more frequent recognition of the disease; however, there are peculiarities of the disease, its methods of transmission and vectors, which make an alarming rate of increase of the disease a definite possibility and danger.

Cause and Mode of Transmission.—Rocky Mountain spotted fever is caused by one of the Rickettsia bodies, *Rickettsia rickettsi.* It is transmitted by at least three species of ticks: *Dermacentor andersoni,* which transmits the severe western variety; *Dermacentor variabilis* or dog tick, which transmits the moderate to severe eastern disease; and *Haemaphysalis leporis-palustris* or rabbit tick, which transmits the disease in rabbits throughout the country and may possibly cause mild infections in man, although there has been no proved case. The life cycle of the tick is an important factor in increasing the prevalence of the disease. *Dermacentor variabilis,* the dog tick, lays from 2,000 to 8,000 eggs on the ground which hatch into the larvae. The larvae attach themselves to small rodents, and after a blood meal, they fall off and molt to the nymph stage. The nymphs again attach to small rodents and then molt again to the adult form. The adults attach to mammals—dogs, cattle, or men. The Rickettsia have been demonstrated in practically all the tissues of the tick, and the infecting agent is transmitted to 50 per cent of the eggs. It is this transmission of the infection from adult to egg, coupled with the reservoir of infection in rabbits transmitted by the rabbit tick *(Haemaphysalis leporis-palustris)*, that makes an increase in the disease in infected areas a strong possibility and the spread of the disease to new localities a probability. A further factor in perpetuation of the disease is the viability of the infected nymph stage of the tick for several months without food; the adult form has been known to live four years without a blood meal.

From the Department of Pediatrics, Duke University School of Medicine and Duke Hospital.

Seasonal Incidence.—Since 1935 eight cases of Rocky Mountain spotted fever in children from 2 to 8 years of age have been treated at Duke Hospital; during the same period only three cases in adults have been treated, which would seem to indicate a higher incidence among children. Of these eight children, two were taken ill in June, four in July, and two in August. The occurrence of these cases coincides with the season of greatest activity of the dog tick; however, unlike the western form of the disease, the eastern variety may occur throughout the year.

Symptomatology.—In our series of eight patients, a history of tick bite was obtained in five, with the onset of symptoms from three to fourteen days later. In five instances fever was the first sign noted. In the other three patients, rash, anorexia, and nausea marked the onset. All of the patients had fever and a rash prior to admission to the hospital, which usually was from the fifth to the seventh day of the disease. In three patients, the rash appeared at the onset of the disease, in three within three days, and in the other two on the fifth and ninth days. The character of the rash at first was macular, gradually became papular, and in about one week after its appearance, was petechial. It faded at the end of the second week and a faint brownish discoloration remained until the end of the third week. On the patients' admission to the hospital, the skin lesions were generalized over the body and extremities, usually including the palms and soles, but in only one patient was a history obtained of the rash starting on the extremities.

The severity of the disease varied from no symptoms, except a rash and fever of 40° C. (104° F.) which fell to normal on the eighth day, in a child of 3 years, to delirium, coma, and a temperature of 40.5° C. in a girl of 6 years. The latter continued to be acutely ill and delirious with fever from 40° C. (104° F.) to 40.5° C. (105° F.) for eighteen days. The average length of fever was fourteen days, and the temperature became normal in all eight patients by lysis during the third week of the disease.

The complications most commonly encountered according to Parker[4] are bronchial, lobar, or hypostatic pneumonia, phlebitis, hiccough, and hemorrhages from the nose, intestine, or kidneys. Only one of our patients had any complications; in this child, aged 6 years, both elbows and the nose became gangrenous, but subsequently healed.

Laboratory and Clinical Diagnosis.—The most commonly used laboratory aid to diagnosis is the Felix-Weil reaction. Agglutination of *Proteus X2* and *X19* organisms by the patient's serum in titers above 1:160 is considered diagnostic. Rocky Mountain spotted fever and typhus fever cannot be differentiated by the Felix-Weil reaction, but can be separated by guinea pig inoculations and biopsy of the skin lesions. The average white blood cell count is from 16,000 to 25,000, with a relative increase in mononuclear cells, but a leucopenia also may occur. Wassermann and Widal reactions occasionally are positive.

In all of our patients the Felix-Weil reaction with *Proteus X19* was positive in dilutions above 1:320. The titer rose at the end of the first week and increased steadily as the disease progressed, so that often by the third week agglutination with *Proteus X19* occurred at 1:1,280 and above. In only three patients was the test positive with *Proteus X2*. Guinea pig inoculations and biopsy of the skin lesions were not done. The average white cell count was 14,000. Two patients had leucopenia with counts of from 5,000 to 6,000.

The differential diagnosis in children is usually between measles, typhoid fever, and typhus fever. The rash in the early stages of the disease very closely resembles that of measles; however, the Rocky Mountain spotted fever may be distinguished by the absence of Koplik's spots and conjunctivitis, and by the fact that, as the disease progresses, the rash becomes petechial. The general appearance of the patient and the high and plateau fever suggests typhoid fever; however, blood cultures are negative, and, as the rash appears, it may easily be differentiated from rose spots. Clinically it is almost impossible, and pathologically quite difficult, to differentiate between typhus fever and Rocky Mountain spotted fever. It is stated that typhus fever is a disease of the winter months and Rocky Mountain spotted fever of the summer months, but as has been mentioned previously, Rocky Mountain spotted fever of the eastern variety apparently occurs throughout the year, while a typhus fever (flea-borne) occurs in endemic form in the summer months. There is little difference in the character of the rash in the two diseases. The rash of Rocky Mountain spotted fever supposedly appears on the extremities, first involving the soles of the feet and palms of the hands and then spreads to the face and trunk, while that of typhus fever is said to appear first on the trunk; however, in all of our patients, the rash was generalized by the time of admission. A definite history of tick bite is of great aid in diagnosis, as typhus is a louse and flea-borne disease. As previously mentioned, a positive differentiation can be made only by guinea pig inoculation tests and biopsy of the skin lesions.

Treatment of the disease is purely symptomatic. The patients should be given careful nursing care to avoid pressure sores, as the disease is a specific endarteritis which renders the skin very prone to ulceration and gangrene. In patients who are delirious the restraints should not be so tight as to cause pressure. Alcohol sponges should be given for temperature above 40.5° C. (105° F.). Liquids with a high caloric value should be "forced," and later a typhoid diet should be given. All of the patients in this series took fluids by mouth very well despite their being delirious. Sulfanilamide and sulfapyridine are definitely contraindicated. The condition of the one patient in this series who was given 2 Gm. sulfapyridine daily for two days became much worse, with fever which rose to 40.8° C. (105.2° F.) and marked accentuation of

the hemorrhagic character of the rash. Later it was reported that guinea pigs with the disease which were given sulfapyridine had a much higher mortality than those which were untreated.[5] Blood transfusions probably also are contraindicated because of the endarteritis; reactions to transfusions have been frequent in these patients. However, if the anemia becomes marked, transfusions may be necessary.

Mortality.—There are no reliable figures on the mortality of the disease in children. The mortality in adults is reported as 25 per cent, with much higher figures, up to 80 per cent, in small areas in the western states. Parker reports a mortality of 37.5 per cent in children in the Bitteroot Valley section of Montana. From our experience the mortality appears to be much lower in children. There were no deaths in this series of eight cases. Dr. A. H. London, Jr.,[6] has treated three children, and Dr. S. F. Ravenel[7] has had thirteen more cases, with three deaths. Shipley[3] reported six cases in children without a fatality, thus making a total of thirty cases with three deaths. However, as shown

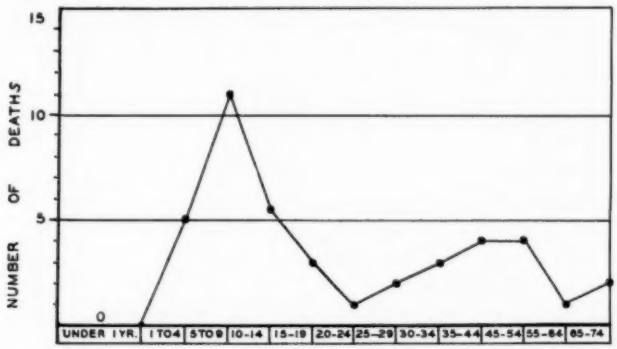

Fig. 1.—Deaths by age distribution for Rocky Mountain spotted fever in North Carolina, 1932-1938.

in Fig. 1, the deaths from Rocky Mountain spotted fever in North Carolina from 1932 to 1938 reach a very definite peak in patients between the ages of 5 and 14 years. This peak is explained probably by the fact that in North Carolina only the fatal cases of Rocky Mountain spotted fever were reported. Undoubtedly the morbidity is much higher in children than in adults. If the true morbidity rate were obtainable, the mortality rate in children would no doubt be lower than in adults.

Prevention.—From a public health standpoint the disease is one which practically defies control on a large scale. Because of the rapid rate of multiplication of the tick, its 2,000 to 8,000 eggs, the transmission of the disease to its progeny, and their extraordinary resistance, it is impossible to exterminate the vector. A vaccine has been prepared by

Spencer and Parker of the United States Public Health Service,[8] which usually protects against the disease for one year and also reduces the mortality among the vaccinated who contract the disease. The cost of the manufacture of the vaccine makes its widespread use impractical. The only feasible method for prevention of infection with Rocky Mountain spotted fever is personal care. Older children should be taught to run their hands across the back of their necks frequently when in low brush and high grass to remove any ticks which may have traveled up their clothing and attached themselves to the skin at the hairline of the neck. They should be cautioned not to pick ticks from dogs, as infection may be contracted by mashing the vector between the fingers. One child 8 years old picked a tick off his younger brother and crushed it between his fingers. Both children developed the disease, the younger child a mild form, but the older child, who had handled the tick, a severe form. Younger children should be examined by the parents every two hours and any ticks removed, as the tick must be attached for at least two hours to transmit the disease. All ticks found should be removed by grasping between the fingers and exerting a steady pull, being careful not to squash the animal. They are most easily disposed of by dropping in a flush toilet. Iodine should be placed in the wound to prevent secondary infection.

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RELATION OF HYPOGLYCEMIA TO THE SYMPTOMS OBSERVED IN INFANTS OF DIABETIC MOTHERS

Report of Six Cases

Herbert C. Miller, M.D., and Ralph A. Ross, M.D.
New Haven, Conn.

THE belief is widely held that the hypoglycemia of newborn infants whose mothers have diabetes mellitus is the cause of the cyanosis, muscular twitchings, convulsions, and, occasionally, the death of the infant. This assumption is naturally based upon the fact that hypoglycemia induced in older patients by the injection of insulin is accompanied by certain well-known symptoms which quickly disappear when glucose is given and the blood sugar concentration thereby returned to normal. However, our experience with infants born of diabetic mothers has given us reason to question whether or not the hypoglycemia so frequently observed in these infants is as significant in the production of symptoms as is generally supposed.

In the past three years six infants born to mothers with diabetes have been cared for by the Pediatric Service from the time of birth to their discharge. In most instances one or the other of us was in attendance at the time of delivery, and in all cases the infants were carefully observed to see whether or not symptoms or abnormal behavior occurred. All six of the infants had very low concentrations of blood sugar during the first day or two of life. In three infants (Cases 1, 2, and 4), symptoms and abnormal findings were present. In no one of these three infants was the administration of glucose effective in relieving the symptoms. More striking than the lack of response to glucose was the fact that in each of these infants evidence of organic disease was found which better explained the symptoms and clinical course than would the hypoglycemia.

We are reporting the cases of the children observed by us because similar findings in infants born of diabetic mothers are not found in the literature.

CASE REPORTS

Case 1.—N. H. H., No. A68045, female. The birth weight was 3,710 Gm. *There were marked hypoglycemia without symptoms and subsequent persistent cyanosis due to acute congestive cardiac failure with recovery.* The mother was 39 years old. Two previous pregnancies had resulted in stillbirths. She was known to have had diabetes mellitus for at least one year prior to the present pregnancy. The diabetes was regulated throughout the pregnancy by diet alone. The Kahn test on her blood was negative. A fasting blood sugar level in the third month of gestation was 0.202 per cent. Pregnancy was uneventful, labor was easy, and delivery was normal

From the Department of Pediatrics, School of Medicine, Yale University.

and spontaneous. Artificial respiration and a mixture of 5 per cent carbon dioxide and 95 per cent oxygen were administered for ten minutes before the infant's respiration became normal. Physical examination at birth was not remarkable.

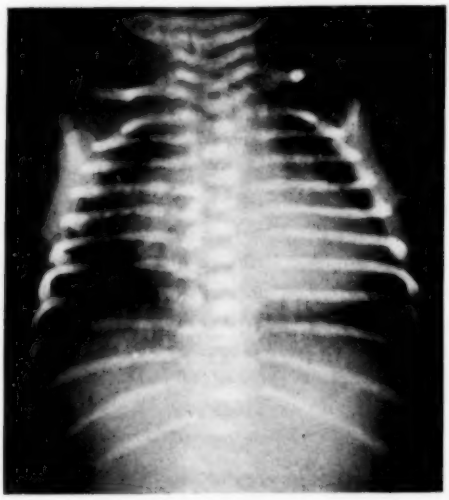

Fig. 1.—Case 1, sixth day of life. Transverse thoracic diameter, 10.1 cm.; transverse cardiac diameter, 7.3 cm.

Fig. 2.—Case 1, sixth day of life. Lateral view.

Repeated mild cyanotic spells occurred during the first twenty-four hours; no therapy was required. At 38 hours of age the blood sugar was zero. Five per cent glucose

in normal saline was given every two hours by mouth. Further cyanotic spells were not noted. A second blood sugar reading on the second day was 0.026 per cent. Four days after delivery the infant suddenly became cyanotic, and the respirations increased to 100 per minute. Five grams of glucose in 10 per cent solution were given intravenously without any alteration in the infant's condition. The infant was placed in an oxygen tent. The next day cyanosis persisted with the baby out of the oxygen tent. A few râles were heard at the bases of both lungs. The heart size was indeterminate, and the liver was palpated three fingerbreadths below the costal margin. A portable x-ray examination of the chest showed a tremendous enlargement of the transverse diameter of the heart. On the sixth day after delivery the infant still had marked cyanosis of the face and sacral regions when out of the oxygen tent. Respirations were rapid, and the cry was feeble. The area of cardiac dullness was thought to be increased and the heart rate more rapid than usual. No murmurs were heard, and the heart sounds were not considered to be abnormal. The liver edge was palpated four fingerbreadths below the costal margin.

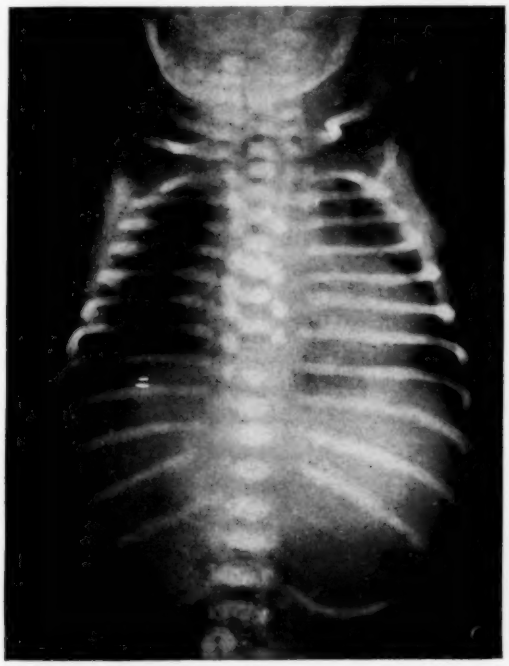

Fig. 3.—Case 1, tenth day of life. Transverse thoracic diameter, 10.7 cm.; transverse cardiac diameter, 7.2 cm.

Some edema of the legs was present. The blood sugar level on this day was 0.075 per cent. Roentgenologic examination of the chest made at five feet showed the transverse diameter of the heart to be very wide (Figs. 1 and 2). On the eighth day the infant was able to remain outside the oxygen tent with only minimal cyanosis. An x-ray examination of the chest on the tenth day showed a decrease of 0.1 cm. in the transverse diameter of the heart shadow (Fig. 3). On the sixteenth day of life, a fourth x-ray examination of the chest showed a further decrease in the transverse diameter of the cardiac shadow of 1.3 cm. (Fig. 4). Findings of the physical

examination of the infant on discharge two days later were normal. The infant was readmitted to the hospital at the age of 3½ months with bronchopneumonia. Physical and x-ray examination of the heart revealed no abnormality. When the infant was last seen at the age of 2 years and 2 months, physical examination again showed a normal infant.

Blood counts on the fourth, sixth, and eleventh days were normal except for the fact that 15,900 and 6,720 normoblasts per c.mm. were counted on the fourth and sixth days; none were seen on the eleventh day.

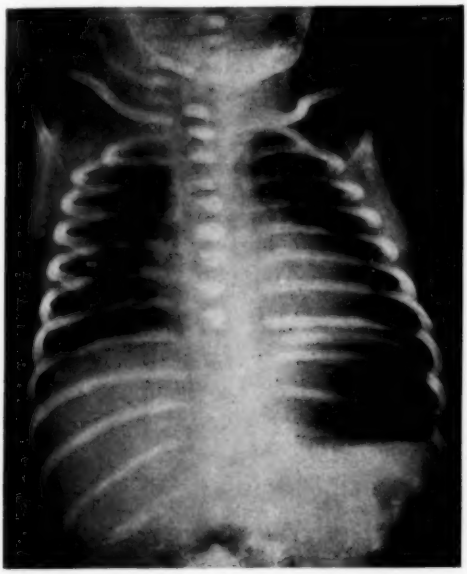

Fig. 4.—Case 1, sixteenth day of life. Transverse thoracic diameter, 10.0 cm.; transverse cardiac diameter, 5.9 cm.

CASE 2.—N. H. H., No. A68553, male. The birth weight was 4,580 Gm. *There was moderate hypoglycemia with symptoms, which were unimproved by the administration of glucose. The symptoms were possibly due to congestive heart failure.* The mother was a primipara who had had diabetes mellitus for two years. The diabetes was controlled without difficulty of any sort throughout her pregnancy by the daily use of 35 to 40 units of regular insulin. The Kahn test on the mother's blood was negative. Delivery was effected three weeks before the expected date by cesarean section. The infant cried spontaneously on delivery. Twenty minutes later he became limp and his cry feeble. Respirations were grunting in character. No cyanosis was present. On physical examination at this time the lungs were clear, the heart was normal, and the edge of the liver two finger-breadths below the costal margin. The blood sugar concentration at 2 hours of age was 0.033 per cent. Seven and one-half grams of glucose by gavage and 1 Gm. intravenously, administered at 2½ hours of age, were without effect on the symptoms. Even though the blood sugar concentration was raised to 0.095 per cent at 4 hours of age, it was not until the infant was 6 hours old that any improvement was noted. The liver, which was observed to extend 7 cm. below the costal margin at 4 hours

of age, was definitely smaller at 24 hours of age, by which time the infant was active and vigorous. The rapid change in the size of the liver was the sole evidence of cardiac failure in this infant. Roentgenologic examinations of the chest were made on the first, third, and seventh days of life to determine the size of the heart. Because of differences in technique from one examination to another, no valid conclusions could be drawn. The infant, when last seen at 2 years of age, was entirely normal, and physical examination was not remarkable.

CASE 3.—N. H. H., No. A75948, male. The birth weight was 4,720 Gm. *There was moderate hypoglycemia without symptoms.* The mother had diabetes mellitus for one year preceding this pregnancy, her fourth. The diabetes was regulated without incident by diet alone for the first six months and by insulin during the last three months. The Kahn test on the mother's blood was negative. Labor was easy and delivery normal and spontaneous. Physical examination of the infant was not remarkable and his course in the hospital uneventful. The blood sugar concentration was 0.0375 per cent at 3½ hours of age, and three more determinations during the first twenty-four hours of life were between 0.069 and 0.089 per cent. A blood count done on the second day of life was within normal limits. A follow-up examination of the infant at 14 months of age was not remarkable.

CASE 4.—N. H. H., No. A76059, male. The birth weight was 2,650 Gm. *There was moderate hypoglycemia with findings suggesting erythroblastosis fetalis and cerebral injury.* This was the first pregnancy of a mother found to have diabetes mellitus during the third month of gestation. The diabetes was regulated without incident by from 50 to 95 units of regular insulin daily after the fourth month. The Kahn test on the mother's blood was negative. The infant was born after the application of low forceps, labor having lasted forty-eight hours. The amniotic fluid was meconium-stained. The placenta appeared normal on gross inspection. The physical examination shortly after birth was not remarkable. The concentrations of blood sugar during the first twenty-four hours were as follows: cord blood, 0.150 per cent; two hours, 0.077 per cent; four hours, 0.036 per cent; seven hours, 0.031 per cent; twelve hours, 0.027 per cent; and fifteen hours, 0.091 per cent. At 12 hours of age, jaundice was first noted. Two hours later the baby became cyanotic. The cyanosis was readily relieved by the administration of a mixture of 5 per cent carbon dioxide and 95 per cent oxygen. Glucose was given by mouth and intramuscularly, but not until the cyanosis had disappeared. The red blood cells decreased from 6,530,000 per cubic millimeter on the the first day of life to 4,270,000 on the third day. The early appearance of jaundice, the rapid fall in red blood cells, the increase in nucleated red blood cells from 880 to 4,600 per cubic millimeter from the first to the second day, and a count of thirty-five normoblasts per hundred white blood cells on the third day suggested that the infant had erythroblastosis fetalis. The infant received 50 c.c. of citrated whole blood in each of two transfusions on the third day. Enlargement of the liver and spleen was not observed. Otherwise than as just noted, the infant's course in the hospital was uneventful during the first ten days. Roentgenologic examinations of the chest made on the second and twenty-first days were not remarkable. Beginning on the tenth day, the infant had repeated convulsions and cyanotic spells for forty-eight hours. The anterior fontanel was bulging and tense. The spinal fluid obtained by lumbar puncture was clear and yellow with a 4+ Pandy reaction; eleven noncrenated red blood cells and fourteen white blood cells per cubic millimeter were counted. The fontanel became definitely softer after the lumbar puncture. It remained soft after the second tap. With repeated lumbar punctures, the Pandy reaction of the fluid decreased, and the fluid became less yellow. The clinical impression was that the patient had had erythroblastosis

fetalis and possibly a cerebral injury as a result of the long labor. Physical examination at 20 months of age was negative for significant findings.

CASE 5.—N. H. H., No. A76445, female. The birth weight was 3,650 Gm. *There was severe hypoglycemia without symptoms.* The mother had had diabetes mellitus for two years preceding this pregnancy. Regulation of the diabetes by the daily injection of from 20 to 50 units of regular insulin was without incident throughout the pregnancy. The Kahn test on the mother's blood was negative. Delivery took place a month before the expected date. Physical examination was not remarkable, and the course in the hospital was uneventful except for a generalized decrease in muscular tone during the first day. Blood sugar concentrations were as follows: cord blood, 0.246 per cent; forty-five minutes, 0.102 per cent; three and one-half hours, less than 0.010 per cent; four hours, less than 0.010 per cent; six hours, 0.017 per cent; nine hours, 0.023 per cent; twelve hours, 0.017 per cent; twenty-one hours, 0.049 per cent; and thirty-one hours, 0.107 per cent. Roentgenologic examinations of the chest on the first and tenth days of life revealed no unusual findings. A blood count made on the second day of life was normal except that a large number of normoblasts (number not stated) was seen on the blood smear. Follow-up examination at 6 weeks of age was not remarkable.

CASE 6.—N. H. H., No. A78473, female. The birth weight was 3,545 Gm. *There was moderate hypoglycemia without symptoms.* This was the first pregnancy of a woman who had had diabetes mellitus for three years. Regulation of her diabetes by daily injections of from 60 to 70 units of insulin a day was uneventful except that three or four mild shocks occurred in the last month of gestation. A moderate toxemia of pregnancy was observed during the last week. The Kahn test on the mother's blood was negative. Delivery occurred at term and was normal and spontaneous. Physical examination was not remarkable, and the course in the hospital was uneventful. Blood sugar concentrations were as follows: cord blood, 0.056 per cent; thirty minutes, 0.035 per cent; two hours, 0.038 per cent; four hours, 0.037 per cent; eight hours, 0.024 per cent; and eleven hours, 0.028 per cent. Roentgenologic examination of the chest made routinely on the seventh day was not significant for any abnormal findings. A blood count on the day of birth was normal except for the presence of eight nucleated red blood cells per hundred white blood cells. Follow-up examination at the age of 2 months was not remarkable.

DISCUSSION

Without more facts than are at present available, a discussion of the effect of hypoglycemia on the newborn infant must be largely of a conjectural nature. Two facts do stand out. Low concentrations of blood sugar are to be expected in infants born of diabetic mothers, and difficulties seem to occur more frequently in these infants than in infants whose mothers do not have diabetes mellitus. There are several reasons for believing, however, that the relation of the hypoglycemia to the symptoms in these infants is not a causal one. If the hypoglycemia is of any significance at all, its role must be more complicated than is at present comprehended.

It has been our observation that low concentrations of blood sugar are occasionally found in infants who presented no abnormal findings in the neonatal period and whose mothers did not have diabetes mellitus.

In Table I are given the results of some studies made by us on the blood sugar of seventeen full-term and twenty premature infants. These are compared with our observations in the six newborn infants of diabetic mothers.

TABLE I

BLOOD SUGAR CONCENTRATIONS DURING THE FIRST 48 HOURS OF LIFE IN NORMAL FULL-TERM AND PREMATURE INFANTS COMPARED WITH THOSE IN NEWBORN INFANTS OF DIABETIC MOTHERS

	FULL-TERM INFANTS	PREMATURE INFANTS	INFANTS OF DIABETIC MOTHERS
Number of infants	17	20	6
Number of determinations	28	40	17
Blood sugar*	0.0499% ±0.0125	0.0318% ±0.0124	0.0297% ±0.0120

*Average blood sugar and the standard deviation from the mean are given.

The average blood sugar concentration* in infants born of diabetic mothers (0.0297 per cent) is significantly lower than in normal full-term infants (0.0499 per cent).† Some of the blood sugar concentrations in the latter group of infants, however, are as low as 0.038 per cent, which is within the limits of the observations in infants of diabetic mothers. It is of interest that the blood sugar concentration in normal premature infants (0.0318 per cent) averages practically the same as that of infants whose mothers have diabetes. The range of blood sugars in premature infants also follows that of the latter group of infants. The above findings are in agreement with those of other investigators, with the exception that the blood sugar concentrations in our study are generally lower than those usually reported.[1-4] This is probably due to the fact that most of the nonglucose reducing substances in the blood were removed in the method used by us. The absence of symptoms in normal infants with low blood sugar levels indicates that newborn infants, in general, adjust themselves without difficulty to low concentrations of blood sugar.

If the same factors were operating to produce symptoms in newborn infants with hypoglycemia as are thought to operate in older patients in insulin shock, one would expect a quick response to the administration of glucose, as is noted in older patients. In Cases 1 and 2 of our series, large amounts of glucose were given when symptoms appeared,

*The method employed in determining the blood sugar concentrations consisted in collecting a little more than 0.2 c.c. of capillary blood in a small glass receptacle containing sufficient dried potassium oxalate to prevent clotting. Two-tenths cubic centimeters was measured out, and the red blood cells laked and the proteins precipitated according to Somogyi's second micro method.[5] To precipitate blood protein 0.175 N NaOH was used instead of 0.15 N NaOH as Somogyi recommended. The extra NaOH was necessary to prevent the occasional formation of a cloud when the ferric iron solution was added. After precipitation of the proteins, the material was filtered through Whatman paper No. 41H. Duplicate analyses were made on 2 c.c. of filtrate by the method described by Folin and Malmros.[6] The color of the final solution was compared with that of a known standard in a photoelectric colorimeter immediately upon formation of the color.

†The difference between the two means is more than five times the square root of the sum of the squares of their respective standard errors.

but without any improvement. In the third infant (Case 4), the cyanosis cleared rapidly with the administration of a mixture of carbon dioxide and oxygen. This failure to observe a response to the giving of glucose in infants with hypoglycemia is striking in the reports by Higgons,[7] Hartman and Jaudon,[8] and Randall and Rynearson.[9, 10] In older patients with hypoglycemia caused by an overdose of insulin, symptoms and abnormal findings may persist for hours, or even days, after the blood sugar has been restored to normal.[11] This delay in recovery is, however, the exception among patients with diabetes mellitus, whereas in infants with hypoglycemia it seems to be the rule.

The fact that, in each of the three infants with symptoms, evidence of organic disease was found which could account for the symptoms (Cases 1, 2, and 4) greatly weakened our belief that the hypoglycemia was the factor directly responsible in their production. In Case 1, evidence of severe congestive heart failure was present. In Case 2, similar, though less striking, evidence of congestive heart failure was found. In Case 4, erythroblastosis fetalis was considered as a possible diagnosis and might have accounted for the early cyanosis. The subsequent convulsive episodes were thought to have been most likely the result of some cerebral injury that occurred at birth.

We wish to call particular attention to the roentgenologic findings in Case 1. Both the enlargement in the transverse diameter of the heart and the subsequent decrease of 1.4 cm. in this diameter in a period of ten days (Fig. 1) were observed after that period in neonatal life when small decreases in the size of the heart may normally be expected.[12, 13] The technique was sufficiently similar from one examination to another that the results may be interpreted with confidence in this instance. Roentgenologic studies were made of the chests to determine the size of the hearts in the remaining five cases, but either the technique was not comparable or no abnormalities were discernible in the case of these infants. Roentgenologic studies of the chest at intervals of a few days would seem warranted in infants with cardiac or respiratory difficulty who were born to diabetic mothers.

We were interested to observe the rather large number of nucleated red blood cells in Cases 1, 4, and 5, with a clinical picture in Case 4 that suggested the possibility of erythroblastosis fetalis. In the small number of infants born of diabetic mothers who have been examined at post-mortem, there are three instances in which large numbers of islands of hematopoietic tissue have been found in the liver.[14, 15] Whether these findings are merely incidental or whether they designate some disturbance of the hematopoietic tissue will have to be decided by future investigations.

SUMMARY

The histories and findings in the cases of six newborn infants whose mothers had diabetes mellitus have been presented.

It is suggested the hypoglycemia present in each infant had no direct and simple relation to the symptoms observed, and the reasons for this suggestion are discussed. The symptoms and clinical courses could, in each instance, be better explained on the basis of organic disease. Acute congestive heart disease occurred in two infants with recovery. A third infant possibly had erythroblastosis fetalis and probably a cerebral birth injury.

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CONGENITAL HYPOPLASIA OF THE MANDIBLE

H. H. Weisengreen, D.D.S., and E. D. Sorsky, M.D.
Fresno, Calif.

ALTHOUGH several diseases are recognized as causative agents in cyanotic attacks in newborn infants, pronounced micrognathia as a clinical entity is not always regarded as a diagnostic possibility. Nevertheless, our case and reports that have appeared in the literature from time to time seem to point conclusively to a congenital malformation as solely responsible for this condition in some instances.

CASE REPORT

A female infant was delivered by cesarean section at the General Hospital of Fresno County. The parents were healthy, and their history was without significant data. The child was born at term and weighed 7 pounds. While it was apparent at once that the lower jaw was grossly retracted, the maxillae, dental ridges, and temporomandibular joints gave every evidence of being normal. No birth injury had occurred.

Fig. 1.—Case of congenital hypoplasia of the mandible.

Shortly after birth, respiratory difficulties were noted, and examination showed the tongue to be resting almost against the posterior pharyngeal wall. All efforts to relieve the dyspnea by postural changes failed, and the choking fits increased in severity. This led us to transfix the tongue in the hope of giving temporary relief, even though we realized the general inadvisability of this procedure. However, despite strong supportive treatment including sedation and glucose, the infant died fifty-two hours after birth (Fig. 1).

Cases of congenital hypoplasia or agenesis of the lower jaw are a well-recognized deformity, characterized by extreme retraction of the

From the General Hospital of Fresno County.

mandible as a whole, and should be distinguished carefully from atrophy of the jaws which occurs in previously healthy and normally developed bone. The condition is noted at birth or soon after. The dwarfed development in the inferior maxilla causes a retracting chin while the upper jaw projects forward and slopes outward, thus emphasizing an abnormal relationship. Since seemingly little progress has been made during the centuries in our etiological conception of embryoplastic deformities, the actual causal agency of this retardation of the lower jaw remains obscure.

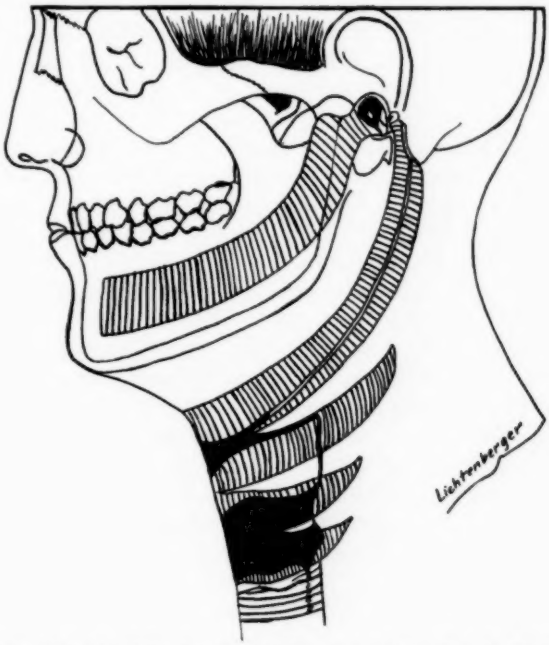

Fig. 2.—Metamorphosis of the five branchial arches. (According to Wiedersheim.)

If we review briefly the embryology of the parts concerned, we recall that from the twenty-fourth to the twenty-ninth days of fetal life the face is undergoing development. Projections grow out from the lateral boundary of the cephalic extremity toward a median line; these are called branchial arches. The superior arch, which with the frontonasal process is destined to form the face, presents secondary protuberances that become the mandibular arch. These are followed by maxillary processes which form at the dorsal part of the mandibular arch and grow ventrally. Hence, anatomically, we may assume that this malformation is peculiar to the first branchial arch. No evidence has appeared to indicate that this retardation of growth affects the branchial arches which comprise the bony structure of the adjacent region (Fig. 2).

Any situation which can influence adversely intrauterine life may prevent unification or coalescence of the branchial arches with resultant deformity. Gladstone and Wakeley have found collaboration for their belief in a pathologic origin created by deficient developmental vigor resulting from malnutrition of the fetus which may or may not include a toxic factor. Thus, from the standpoint of transmission, a disease state in the mother which causes a depressed growth impulse through defective nutrition is the inherited factor rather than the actual deformity.

On the other hand, several investigators, among them Davis and Dunn, express the opinion that these conditions may result from mechanical occurrences alone. This grouping would include not only the intrauterine stage, but the period of birth as well. In the uterus, pressure brought about by the increasing weight of the fetal body normally placed could easily effect the relative positions of the ununited maxillae and, at the same time, retard natural development. This explanation would seem to be strengthened in these cases by the frequent accompaniment of facial clefts which are known to be due to a failure of the maxillary processes to meet and unite. In this connection, too, it seems probable that abnormal positions in utero produce inhibitory effects on growth. Still within this division may be added the traumatic injuries incidental to birth. Thoma has recorded instances of mandibular hypoplasia attributable to this cause.

In these conditions, the shortened lower jaw and accompanying inadequate musculature in the submaxillary region do not retain the tongue in a position sufficiently forward to permit normal breathing. Therefore, when the deformity is particularly marked, as it was in our case, the tongue falls back against the posterior pharyngeal wall, and efforts of a temporary nature must be directed toward the maintenance of an air passage. Occasionally this is accomplished by keeping the infant in a position, usually face downward, that tends to overcome the effect of suction in breathing which pulls the tongue backward. When postural measures fail, however, more drastic means are attempted to avert the otherwise hopeless outcome.

Equally important is the necessity for establishing satisfactory feeding. The baby is frequently unable to grasp a nipple because of the uncontrolled tongue. Moreover, the opened mouth, constant salivation, and inability to swallow make attempts at artificial feeding dangerous. The situation is further jeopardized when a cleft in the lip or palate is present, a circumstance reported in the majority of cases. In addition, the enforced mouth breathing sends air into the bronchi unwarmed by passage through the nose, and a stimulus to respiratory affections is set in motion.

When the deformity is less severe, a partial air passage is maintained as well as indifferent success with feeding. Since, however, the baby

usually gets only a portion of the nourishment required in this way, the physical condition becomes progressively worse, and medical aid is sought after malnutrition is in an advanced stage. Here, as in those cases requiring immediate therapy, every effort must be made to have the infant receive sufficient nourishment. The daily growth of the hard and soft tissues of the face will sometimes prove to be the only treatment needed. Lenstrup reported the case of a girl brought to the hospital at the age of 6 weeks. They were able to overcome feeding difficulties, and the growth following adequate nutrition so improved the musculature in and under the tongue that the organ remained forward in normal position.

The importance of the role played by the tongue in Robin's estimation may be surmised when, in a more recent article, he quoted himself as having first used the term "glossoptosis" in 1923. Both he and Lapage emphasize the influence of the nursing mother's posture, and use as an illustration the fact that the young of certain mammals reach up to nurse. In explaining what he called orthostatic feeding, Robin says, "The baby sucks with his thorax held up straight so that he lifts his neck and propels his chin forward. . . . In order to feed her child orthostatically the mother is obliged to hold herself erect, with the breast elevated and the thorax held up." Otherwise, the weight of the breast has a tendency to rest on the child's chin. This idea of feeding an infant in a manner that will enforce action in the muscles of the lower part of the face has been applied also by Davis and Dunn, who attached to a nursing bottle a curved plate that rested against the infant's upper lip. This plate, being freely movable, could be regulated to make the child extend the lower jaw.

Types of apparatus much more complicated than this have been devised and have found favor with some physicians. Eley and Farber constructed a brace that "consists of a strong piece of copper wire which rests on a soft flannel band as it passes across the forehead and which is shoed with rubber tubing as it passes down the side of the jaw. Here it passes under the ramus, forming a right angle to the descending limb. The two ends of the frame are then joined by a piece of white tape which holds the frame firmly in position and tends to maintain the pressure that is exerted against the mandible and the floor of the mouth. The mandible is then displaced forward and, at the same time, pressure is exerted against the floor of the mouth and the base of the tongue." They claim satisfactory results with this apparatus.

Callister is under the impression that his application of skeletal traction to the correction of micrognathy in an infant is unique. An apparatus resembling the jury-mast used for fractured cervical vertebrae was strapped to the child. From this a large flat aluminum ring was brought around in front of the baby's mouth. Arranged with a spiral

spring to allow some movement, "a thick silver wire was passed through the skin and around the mandible" and fixed to the metal band. According to the author, the child wore this for four weeks, after which it was no longer needed; she was discharged in excellent condition.

CONCLUSION

Cases of congenital hypoplasia, it appears, require either emergency treatment from the time of birth to maintain respiratory adequacy or, when the deformity is less severe, therapeutic intervention after a period of days or weeks in cases where insufficient nutrition has inhibited normal development.

Measures designed to correct the deformity by nonoperative methods as soon as the baby's physical status permits have been found preferable to surgical or mechanical procedures carried out later in life.

While various forms of intricate apparatus have been devised and have been reported upon favorably, they have failed in many instances, owing to the restricted area of application, the tenderness of the tissues involved, and the danger of increasing respiratory obstruction.

With the exception of emergency measures, treatment, it would seem, is most successful when directed toward the establishment of a natural bodily development in the child in order to encourage growth in the underdeveloped region.

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ACTINOMYCOSIS

Report of a Case in a Child With Recovery Following Thymol Therapy

Harry H. Clemens, M.D.
Louisville, Ky.

RECENTLY several cases of actinomycosis with recovery under sulfanilamide have been reported (Miller and Fell, Hall). The following report illustrates the case of a patient in whom sulfanilamide was of little avail, but who recovered under thymol administration.

Human actinomycosis appears to be widespread over the world, as reports of cases of actinomycosis in the adult, as well as in the child, have been published in almost every civilized country. In the European literature at least one thousand articles have appeared (Cope). On the other hand, reports of cases of actinomycosis in the American literature are relatively uncommon. Murphy, in 1885, seven years after Israel's initial report in Germany, described the first human cases in America. Four years later Ruhräh collected a series of sixty-two cases in the United States. Sanford and Voelker's survey in 1925 embraced 670 cases of the disease that had occurred in this country (including Mayo Clinic's and Ruhräh's cases). In 1931 Figi and Cutts gathered together a total of 450 cases of actinomycosis that had been studied at the Mayo Clinic. Rarity of the disease in man is indicated from an examination of the 141,064 admissions to the Louisville City Hospital from 1923 to 1938, where only six patients have been diagnosed as having an actinomycotic infection.

It is unusual to find the disease in a child. Accounts of the disease are found only in the larger reference books (Brennemann, Abt.). Edwards reviewed the literature and reported on five cases of actinomycosis in children which he had investigated. Figi and Cutts included fourteen children (3 per cent) in their large series. About 6 or 7 per cent of the patients in Sanford and Voelker's extensive review were children. The incidence of the infection in children below 10 years of age is generally given at about 3 per cent (Cope, Brennemann).

Actinomycosis may affect the infant as well as the child. The youngest patient reported was a 28-day-old marasmic infant who died with an actinomycotic pulmonary abscess.

Alfred S., negro male, aged 10 years, was admitted to the Pediatric Service of the Louisville City Hospital Nov. 17, 1938, with the chief complaint of swelling of the glands of the neck. The onset was dated at one month previously when the patient had an upper respiratory infection accompanied by a cough. One week

From the Bacteriological and Serological Laboratories of the Louisville City Hospital and the City of Louisville Department of Health.

after onset of the "cold," bilateral enlargement of the cervical lymph nodes occurred, chiefly on the left side where it became extensive and migrated anteriorly. In the interim the patient did not appear to have any fever, did not appear ill, and played about as usual. There were no other complaints except for tenderness over the swollen areas.

The patient was an only child of apparently healthy parents. His birth and infancy were uneventful except for otitis media, tonsillectomy, and the drinking of coal oil with no untoward results. This child was apparently well up to the onset of his present illness. The mother of the patient is syphilitic and now under treatment.

Examination.—The patient was a fairly well developed and well nourished negro male child who did not appear to be in any discomfort or distress. Temperature was 100° F., pulse rate 92, and respiratory rate 24. On the left lateral aspect of the neck a mass, approximately from 3 to 4 cm. in width, which was firm, indurated, and slightly tender, extended just posterior to the angle of the jaw and medially to the upper border of the thyroid cartilage; the mass was not fluctuant, but felt more solid than the usual adenopathy in septic or tuberculous adenitis. It was thought that the right cervical nodes were in the mass. A chain of cervical nodes was palpable on the right; the left axillary nodes were also palpable. The teeth were dirty and carious, with the first permanent molar in the left mandibular region, the second deciduous molars of the right mandibular and the upper left arch, and the deciduous canine and deciduous first and second molars being principally affected. The tissues of the mouth appeared to be normal and of good color. The tonsils were absent. There was no rigidity of the neck. The lungs were essentially normal. Except for a suggestive soft systolic murmur to the left of the sternum at the level of the third interspace, the heart was negative on examination. Neither the spleen nor the liver was palpable. No cutaneous lesions were present. The clinical diagnosis was: (1) adenitis of the left cervical nodes (etiology?), and (2) dental caries.

Laboratory Data (First Admission).—On the day of admission (Nov. 17, 1938), the urine was essentially normal. The blood count revealed 5,950,000 red blood cells, with hemoglobin of 12 Gm. per 100 mm. The white blood count was 15,250 per cubic millimeter. A differential blood count two days after admission showed polymorphonuclear leucocytes, 54 per cent, lymphocytes, 22 per cent, eosinophiles, 14 per cent, monocytes, 9 per cent, and basophiles, 1 per cent. Several other differential counts made after this showed the eosinophiles to vary from 8 to 14 per cent. The Kahn reaction of the blood was negative. The Paul-Bunnell test, to eliminate a possible acute mononucleosis, was in the titer of 1:8 and within normal range. Throat cultures (Nov. 17, 1938) for hemolytic streptococci and diphtheria bacilli were negative. A blood culture taken on November 20 revealed no growth after three weeks. The Mantoux test with old tuberculin, 1:1,000 (Nov. 17, 1938) was negative. Roentgenologic examination (Dec. 12, 1938) showed the chest to be negative. There was a soft tissue swelling of left side of neck, and the cervical spines were negative.

Course.—The temperature range during the first week after admission was essentially normal, with only an occasional afternoon rise to 100° F. The lesion on the left cervical region was hot-packed during this time and became slightly fluctuant. The patient was then referred to the surgical service for drainage of the cervical mass. Under surgical anesthesia aspiration of the mass was attempted without obtaining any pus. A fluctuant area in the lower anterior cervical region was drained, however, releasing about 10 c.c. of bloody, odorless pus. At that time no sulfur granules were noted. Previous to surgical intervention, the possibility of an actinomycotic infection in the patient was suggested.

Bacteriologic Data.—The pus obtained on incision was sent immediately to the

Bacteriological and Serological Laboratories where smears were made, and the material was inoculated into deep meat media (pH 7.6), Douglas tryptic digest broth (pH 7.6), nitrate broth (pH 7.6), tryptone broth (pH 7.6), 5 per cent rabbit blood agar plates, and Sabouraud's plain agar (pH 4.7). The pus was sent to the laboratory on swabs, and the presence of uncrushed sulfur granules was not seen. Smears stained by the Gram method revealed the presence of gram-positive filamentous rods, some of which showed branching. Scattered about the smears were groups of intermeshed gram-positive filamentous elements, surrounded by a gram-negative periphery. These may have been crushed granules. No bacteria were seen. A Ziehl-Neelsen stain of the material showed that the filaments were non-acid-fast.

Growth of inoculated material was slow and appeared only in the anaerobic deep meat and in the Douglas broth tubes. The growth in the latter media was flaky and was limited to the bottom of the tube. Similar growth occurred in the deep meat tubes. The cultures appeared to be uncontaminated. Transfers were made from the original growth to 5 per cent rabbit blood agar plates in Spray anaerobic dishes (pyrogallic acid 5.0 per cent and sodium hydroxide 2.5 per cent were employed for oxygen absorption) so that the colony characteristics could be studied. On the Spray dishes, colonies were apparent after three days; they were grayish-white in appearance, discrete, not adherent, and had nodular surfaces, being from 1 to 3 mm. in diameter. Smears of the colonies revealed them to be made up of actinomyces similar in appearance to that in the original pus.

Cultural activities of the organism were carried out and are summarized as follows: acid production without gas in glucose, lactose, maltose, sucrose, and salicin broths. Indol was produced in the tryptone broth. There was no growth on Sabouraud's medium or corn-meal or prune-juice agars. The best growth occurred in anaerobic media and in Douglas broth. In the latter medium, growth was very good, being granular in appearance with colonies appearing on the sides of the tube almost up to the surface; no pellicle was formed and no turbidity of the broth occurred. In the deep meat media good growth occurred as described above. On Loeffler's media growth was poor, with but slight liquefaction of the coagulated serum. On rabbit blood agar and chocolate agar there was a fair growth of soft grayish colonies. Growth was poor on glucose agar.

On first isolation, the actinomyces were anaerobic; after repeated subcultures fair growth could be obtained under reduced oxygen tension on rabbit blood agar. In the carbon dioxide (10 per cent) jar, good growth resulted.

Aspiration of a fluctuant area of the mass in the left cervical region was performed Dec. 2, 1938, and about 3 c.c. of thick bloody material containing granules was obtained. The granules were light yellow in color; they varied from 1 to 2 mm. in diameter and resembled the "drusen" described in the literature. Some of the granules were moistened in sodium hydroxide (20 per cent) and crushed between cover slips, whereby crystalline structures were evident. Gram stains of the granules revealed the typically gram-positive branching filamentous organisms characteristic of the pathogenic actinomyces. Besides these, numerous gram-negative coccoid bodies in groups were present; these forms resembled the *B. actinomycetum comitans* as described by Wright and Bayne-Jones, but could not be isolated in pure culture.

Growth of the actinomyces was accompanied by a peculiar odor, described by some of the laboratory workers as cheeselike, by others like that of unwashed feet. This odor was more profound in newly isolated cultures, becoming less profound as the colonies became older. Frequent transfers were required to keep the cultures alive. Subcutaneous and intraperitoneal injections of from 2 to 4 c.c. of heavy broth suspension of the organisms into several guinea pigs produced no pathologic changes in the animals. Similar injections in rats and mice produced no pathologic changes.

The actinomyces as described above were isolated for the third time in pure culture, again from tissue taken on biopsy Jan. 4, 1939.

An attempt was made to agglutinate a suspension of the actinomyces with the patient's serum, but with no success. An intradermal injection of 0.1 c.c. of a vaccine (corresponding in density to the barium sulfate standard No. 3 of McFarland's nephelometer) made from the actinomycotic organisms produced a tender area of induration and erythema 12 mm. in diameter on December 19; this reaction disappeared in forty-eight hours. Similar injections given to five other children as controls were negative. Control injections of Douglas broth were negative in the patient as well as in the others.

On December 11 the patient was referred to the dentist for dental extraction. It was felt that a possible focus of the disease lay in the carious teeth and that their removal might facilitate recovery. The upper right deciduous cuspid and the first molar were extracted. The cuspid was sent to the Bacteriological and Serological Laboratories for culture immediately after removal. The molar was eliminated because of gross contamination. Smears of material from the

Fig. 1.—Patient before thymol therapy.

Fig. 2.—Patient after completion of therapy.

cuspid and subsequent cultures revealed gram-negative filamentous elements. Probably because of the heavy contamination with staphylococci, streptococci, and other organisms in the carious tooth, actinomyces were not isolated. No definite gram-positive filaments were ever found.

Therapy (First Admission).—On the day of admission to the hospital 0.6 Gm. sulfanilamide, together with sodium bicarbonate in the same dosage, was given every four hours in the belief that the infection was streptococcic in etiology. This dosage was maintained for twenty-seven days (from Nov. 17 to Dec. 12, 1938, even after actinomyces were discovered in the pus from the lesion) to determine the effect of the drug on the disease. During this chemotherapy, fever up to 100° F. occurred daily as of before. The disease process did not abate. The cervical mass became

fluctuant and broke down, giving rise to a discharging sinus. After two weeks of sulfanilamide therapy, it was decided to employ at weekly intervals, as adjuvant therapy to the sulfanilamide, deep roentgen therapy in doses of 150 R (at 50 cm. without a filter). This was started on Dec. 2, 1938, and was discontinued on Dec. 21, 1938, after a total dosage of 600 R.

Therapy with sulfanilamide and deep x-ray appeared to improve the condition somewhat, for there was a lessening of the drainage and a slight decrease in the size of the lesion. The last x-ray treatment was two days after discharge from the hospital. At that time the pathologic process seemed on the way to improvement; however, it had not yet abated, for a few days after discharge the cervical lesion began to increase in size and became tender again. The patient was, therefore, readmitted to the hospital for further therapy.

Examination (Second Admission, Jan. 3, 1939).—Physical examination was essentially the same as on the first admission, except for the lesion in the cervical region which had become larger and now had four draining sinuses. Sanguineous fluid discharged from each sinus. The cervical mass was slightly red and quite tender to palpation. The actinomycotic process had extended anteriorly to the midline and posteriorly to the region below the left ear; inferiorly it had progressed to the left supraclavicular space. Temperature was 103° F.; pulse rate was 120, and respirations, 30. In general, the patient's condition was worse now than it had been at the first admission.

Fig. 3.—*Actinomyces bovis* from culture. (×1000.)

Laboratory Data (Second Admission).—The urine examination was essentially negative. An examination of the blood on Jan. 7, 1939, revealed 4,100,000 red blood cells and 8,200 leucocytes. The differential blood count showed polymorphonuclears, 59 per cent, lymphocytes, 32 per cent, monocytes, 3 per cent, and eosinophiles, 6 per cent. The Mantoux test was repeated and was negative in a 1:100 dilution of old tuberculin. A roentgen ray of the chest made Jan. 6, 1939, was negative. On Jan. 4, 1939, a biopsy of skin from one of the draining sinuses was performed. Adherent to the sinus tract were a few yellow granules. When placed between cover glasses these granules were seen to be made up of densely packed filaments which exhibited a radial arrangement. Morphologically and culturally they were *Actinomyces bovis* of the Wolff-Israel type and identical to that isolated from the pus on the first admission. The pathologic report on the biopsy revealed that it contained many areas of chronic granulation tissue, showing

dense leucocytic infiltration in one area. The majority of the invading leucocytes were lymphocytes, but there were also large numbers of epithelioid cells, plasma cells, and polymorphonuclears. No typical ray-fungus structures or tubercles were seen.

Therapy and Subsequent Course.—After the second admission it was determined to give 1.0 Gm. thymol daily by mouth. The drug was given in milk one hour before breakfast. The patient was able to tolerate this medication for twenty-eight days without having any nausea, epigastric burning, or other ill effects. From the onset of this therapy the cervical mass began to decrease in size. The sinuses gradually ceased to drain and healed. On Jan. 31, 1939, twenty-eight days after onset of thymol therapy, the cervical mass had practically disappeared. At this time the patient complained for the first time of nausea, epigastric pain, and anorexia. Thymol dosage was then reduced to 0.3 Gm. daily. On February 10, the patient was discharged, the cervical mass having disappeared and all sinuses having healed. Likewise, his general physical condition had improved. The clinical diagnosis at the time of the patient's discharge was actinomycosis of the left cervical region.

Before discharge from the hospital, the patient was again tested intradermally with 0.1 c.c. of vaccine made from the actinomyces isolated from his pus. The reaction obtained was similar to that on his first admission. Control injections in five other children, clinically free of actinomycotic infection, were negative. It was the consensus of opinion that recovery had occurred with the thymol therapy. Follow-up care two months after discharge revealed the patient to be in good health with no recurrence of the disease.

COMMENT ON SOURCE OF INFECTION

The possible source of infection in the case reported above is of interest. A review of the history of the case leading up to the illness revealed the fact that the patient had played about with some sick cows in the vicinity of his home in Highland Park about one year previous to the onset of his infection. According to the mother of the patient, one of the cows died later. She has no knowledge as to whether the animal had "lumpy jaw" or any abscesses about its head or body. This is of interest because animal-to-man transmission of actinomycotic infection, though rare, is not improbable. Osseous actinomycosis of the right index finger in a 22-year-old white male treated at the Louisville City Hospital occurred two weeks after he had cleaned out, with the involved finger, a large abscess in the jaw of his sick cow. Despite occasional cases of proved man-to-man and animal-to-man transmission of the disease, the work of Wright, Lord, Naeslund, and other investigators who have revealed the presence of typical pathogenic actinomyces in the mouths of normal human beings makes one lean toward the theory that trauma and lowered resistance provide the avenues of infection of organisms that are already in the host. Naeslund demonstrated the presence of the *Actinomyces bovis* in the tartar of teeth. Lord isolated actinomyces in the carious teeth and tonsillar crypts of healthy children. In the case reported above, gram-negative actinomycotic filaments were seen in the culture of a tooth; these resembled filaments isolated from the lesion of the patient. No gram-positive filaments, however, were observed in the tooth cul-

ture. The source of infection in our patient is indefinite, but transmission of the disease from the cow has not been ruled out.

COMMENT ON THERAPY

Myers and Thienes, in 1925, showed the fungicidal action of the volatile oil, thymol. They demonstrated that a 1:1,000 aqueous solution of the drug killed actinomyces rapidly and suggested its possible use in the therapeutics of actinomycosis. One year before, Myers had obtained a cure employing the drug in doses of from 1 to 1.5 Gm. orally, twice a week. Later, in 1937, he reported on four other cases which recovered under thymol therapy. In his later cases, Myers increased the dosage of thymol to 1.5 Gm. daily. He advised the local, as well as the systemic, use of the drug. Thymol in oil, in from 10 to 20 per cent strength, was utilized locally for injection of the sinuses. Joyce employed thymol along with radical surgery and believed it the most effective treatment for actinomycosis.

More recently sulfanilamide has made its entry as an actinomycoticide. Walker, in England, reported a case of abdominal actinomycosis cured by sulfanilamide. Miller and Fell also used sulfanilamide with success in the treatment of a progressive case of abdominal actinomycosis. They had previously employed thymol along with potassium iodide and roentgen therapy without causing a recession of the process. Hall, corroborating Miller and Fell, relates a case of pelvic actinomycosis in a young woman which was cured by sulfanilamide given on an empirical basis and in which potassium iodide was of no avail.

In the case reported here, sulfanilamide in the dosage of 1.0 Gm. every four hours over a period of twenty-eight days did not prevent the progress of the actinomycotic process.

SUMMARY

A case of cervical actinomycosis in a 10-year-old colored male child herein reported is of interest because:

1. The diagnosis was made before sinus formation occurred.
2. The organism involved was isolated, cultured, and identified as the *Actinomyces bovis* (of the Wolff-Israel type).
3. Sulfanilamide, as well as deep roentgen therapy, was ineffective in the treatment.
4. Recovery apparently occurred under adequate thymol therapy.

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FULMINATING MENINGOCOCCEMIA WITH BILATERAL ADRENAL HEMORRHAGE

(WATERHOUSE-FRIDERICHSEN SYNDROME)

JACOB A. DANCIGER, M.D.
NEW YORK, N. Y.

INTRODUCTION

THIS syndrome now known as the Waterhouse-Friderichsen syndrome was first recognized in 1901 by Little.[1] Since 1901 several reviews of the literature have been published describing the symptomatology and pathology on the basis of sixty-four case reports (Waterhouse,[2] Friderichsen,[3] Bamatter,[4] Aegerter,[5] Sacks,[6] and Levinson[7]). Within the past two years nine more cases have been described.[8-13] Our own case brings the total number described to seventy-four.

Fig. 1.—Massive bilateral adrenal hemorrhage.

The symptomatology of the syndrome is strikingly uniform and classically demonstrated by our case. Likewise, the pathology in all cases revealed massive bilateral adrenal hemorrhage (Fig. 1). The etiology, however, has been the subject of controversy. Many theories have been proposed, and the most acceptable is one of massive bacterial invasion of the blood stream. Until 1916 the number and variety of organisms cultured from the blood, adrenals, and skin lesions, including streptococcus, staphylococcus, pneumococcus, colon

From the Pediatric Service of Dr. Béla Schick, Chief of Staff, Mount Sinai Hospital.

bacillus, *Bacillus pyocyaneus,* Friedländer's bacillus, etc., would lead one to assume that the described syndrome may have been caused by numerous different organisms. Since 1916, when McLagen and Cooke[14] first isolated the meningococcus from two cases, the literature almost universally implicates the meningococcus as the etiological agent. The work of McLagen and Cooke,[14] McLean and Caffey,[15] Bamatter,[4] and others leaves little doubt that the most frequent causative agent is the meningococcus. Of the seventy-four cases described, 70 per cent were due to massive blood stream invasion by the meningococcus.

This fulminant syndrome usually runs its striking course to death within twenty-four hours or less. Seventy per cent of the patients were under the age of 2 years, and 95 per cent under the age of 6 years.

This is the case of a 3-year-old male child of Italian extraction (V. G.). His family history was essentially negative, and his past history revealed measles, pertussis, chicken pox, and tonsillectomy.

The child had been perfectly well until about 5:30 P.M. on Sept. 6, 1939, at which time, while playing outdoors, he complained to his mother of feeling weak in the legs and having a pain in the right thigh. The mother noticed that the child limped. She took him into the house immediately. Shortly thereafter he had a shaking chill with spastic, somewhat convulsive movements. The mother took his temperature, and it was 103° F. The family physician was called and saw the patient about one and one-half hours after onset of the illness. He could find only a red throat. The child then began to have several more spastic seizures and also vomited several times. About midnight he became lethargic and stuporous and did not respond to the mother's questioning. As the temperature continued to rise, the child was brought to the hospital at about 2:30 A.M., i.e., nine hours after the onset of illness. At this time the temperature was found to be 107° F.

On examining the child we found him in a semicomatose state and unable to answer questions. His general appearance was that of a very well nourished and well developed male child who was practically moribund. There was present marked conjunctivitis; the left eardrum was reddened; the throat was quite red, and a thick mucoid secretion was found in the mouth and pharynx. There was no generalized glandular enlargement. There were no marked changes in the lungs except a few râles which could be heard in the right axilla and over the left lower lobe posteriorly. The heart sounds were very distant and of poor quality. The abdomen was negative except for slight spasticity of the right upper quadrant. Rectal examination was negative. Neurologically, there was evidence of sluggish deep reflexes; abdominal reflexes were absent, cremasteric reflexes sluggish, and Kernig and Brudzinski reflexes questionably positive. There was no nuchal rigidity. There were present a few erythematous macular areas on the neck.

X-ray of the chest failed to reveal any evidence of pneumonic infiltration. Shortly after admission it was noticed that the erythematous lesions, which at first were only on the neck, could now be seen also on the face, chest, and arms.

The blood count revealed: hemoglobin, 80 per cent; white blood cells, 5,000, with a differential of adult polymorphonuclears, 24 per cent, juvenile polymorphonuclears, 7 per cent, lymphocytes, 67 per cent, monocytes, 2 per cent. The spinal puncture was negative except for an initial pressure of 250 mm. The fluid was clear and contained only four cells; Pandy's test was negative.

At about 4:30 A.M., eleven hours after the onset of the illness, the child became very cyanotic and dyspneic. A continuous intravenous injection of 250 c.c. normal saline was given, followed by a blood transfusion of 300 c.c.

The impression was that we were dealing with a fulminating septicemia of unknown type. We had no evidence of meningitis nor of a pneumonia. The smear from the spinal fluid revealed no organisms.

The child went into deep coma and became more cyanotic. The pulse became much faster and threadier, and the respirations, which had been between 50 and 60 per minute, now became very shallow and rapidly developed Cheyne-Stokes character. The skin lesions, which before were macular and erythematous in appearance, now took on a hemorrhagic character which became more conspicuous as the cyanosis deepened. The cyanosis quickly took on a heliotrope color and looked splotchy, just as is seen after death. The heart action became poorer. Cardiac stimulants were given, but the child continued to go downhill very rapidly and died at approximately 8:00 A.M., or fourteen and one-half hours after the onset of illness.

The laboratory reports were as follows:

The sputum revealed pneumococcus Type XIX. The blood culture was positive for meningococcus (30 colonies per cubic centimeter). The spinal fluid culture was negative. The spinal fluid chemistry revealed chlorides, 770 mg. per cent; total protein, 25 mg. per cent; sugar 55 mg. per cent. The tryptophane test was negative; blood serology was negative. Stool culture revealed *B. coli*.

Permission for autopsy was obtained, and prior to the post-mortem examination, a smear was made from one of the purpuric spots which did not reveal the presence of meningococci.

Pathologic findings were as follows:

Gross findings revealed congestion of lungs, hypertrophy of mesenteric lymph nodes, and Peyer's patches. The adrenals exhibited the most important pathologic findings. They were bluish in color and not enlarged. On cut section there was seen gross hemorrhage of the medulla and innermost layer of the cortex. Also some blood was seen in the outer cortical layers. The brain was grossly negative.

Microscopically, the adrenals showed complete destruction by hemorrhage of the entire medulla and the zona reticularis, so that no pigmentation was seen. Only a few scattered parenchymal cells persisted. Some areas of the cortex were not involved. The lungs and liver showed only marked congestion and edema. The hyperplasia of the mesenteric lymph nodes and Peyer's patches were confirmed by microscopic examination. Small areas of hemorrhage were seen in the kidneys and one testis. The skin hemorrhages were located in the fatty layer of the epidermis. No bacteria were found in the purpuric areas. Microscopic examination of the brain revealed no abnormalities in the leptomeninges. Special stains showed gram-negative diplococci within the leucocytes contained in the meningeal vessels.

COMMENT

The diagnosis of this syndrome should be considered in all infants and young children who become suddenly ill with vomiting, diarrhea, and collapse, particularly if the illness is associated with high fever, purpura, and cyanosis. It must be differentiated from other causes of adrenal hemorrhage, such as hemorrhage of the adrenal occurring in the newborn infant, or traumatic adrenal hemorrhage, which are usually not associated with purpura. There should be little difficulty in differentiating the syndrome from such conditions which have been

known to cause adrenal hemorrhage, such as diphtheria, scarlet fever, smallpox, and, occasionally, measles and pneumonia. Massive hemorrhage in the adrenals occurs in guinea pigs after injection of diphtheria toxin. This form of massive adrenal hemorrhage is not seen in diphtheria of the human being. However, the adrenals do show definite pathology. Greater difficulty in diagnosis may be encountered in districts where violent toxic scarlet fever or hemorrhagic smallpox occurs, for these diseases may produce a picture similar to this syndrome. The presence of meningococci in the smear of the purpuric spots (Fig. 2), as pointed out by McLean and Caffey, will certainly facilitate the diagnosis.

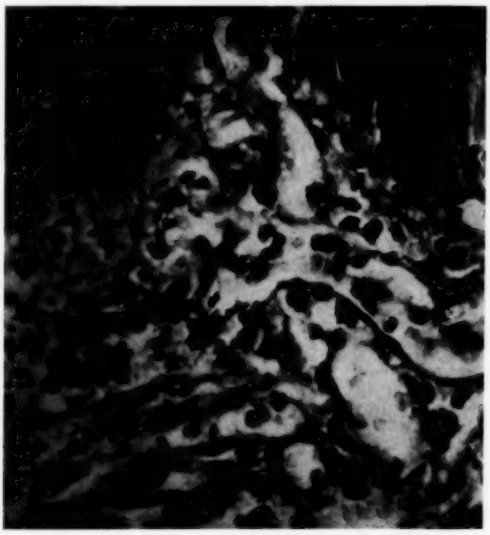

Fig. 2.—Section through purpuric spot showing dilatation of blood vessels and presence of meningococci within these vessels.

Up to the present time, the prognosis is fatal.

Because of the very fulminant course of the syndrome, the therapy has been, to a great extent, based upon theoretical grounds. There is hope, however, that some of these cases may be saved if the diagnosis is made early enough. Sulfanilamide, intravenous antimeningococcus serum, intravenous saline, transfusions, adrenalin, and cortical extract should be used before the laboratory corroborates the suspected diagnosis.

SUMMARY

A case of a patient with the Waterhouse-Friderichsen syndrome has been described.

Seventy-four such cases have been described in the literature. Ninety-five per cent of the patients have been under 6 years of age.

The etiology has been shown to be the meningococcus in 70 per cent of the cases.

Symptomatology is strikingly uniform, with sudden onset, restlessness, and gastrointestinal symptoms, followed shortly by cyanosis, purpura, lethargy, coma, high fever, and death. Death occurred within twenty-four hours or less in the majority of cases.

Massive bilateral adrenal hemorrhage is the most common autopsy finding.

Suggested therapy includes sulfanilamide, antimeningococcus serum, intravenous saline, transfusions, adrenalin, and cortical extract.

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EPIDERMOLYSIS BULLOSA HEREDITARIA

GEORGE M. WADDILL, JR., M.D.
AMARILLO, TEXAS

EPIDERMOLYSIS bullosa hereditaria is not often seen, but because its lesions are so similar to those of pemphigus neonatorum, it may on occasion present a diagnostic problem in the nursery. This condition is said to have been first described by Goldschneider in 1882. Its symptoms are brought about by a hereditary peculiarity of the skin characterized by an absence of, or decreased amount of, the elastic tissue of the skin. The case reported here is interesting both because of the symptoms manifested and because the hereditary tendency for the disease is traced through a person whose fraternal twin escaped being affected.

J. E. P., white male infant, was first seen Nov. 12, 1938, at the age of 4 days, with the following history.

At birth the infant appeared normal. On the second day a smooth, red, macular rash appeared on the body, and there were two or three small yellowish bullae on the face and a large yellowish bullous lesion on each heel. The lesions on the heels were about the size of pigeon eggs. They were incised, and a yellowish exudate was liberated.

On the third day the infant was circumcised, and the mother was allowed to leave the hospital and take the baby with her. Four hours later the patient was readmitted because of free bleeding from the site of circumcision. At this time a new blister was discovered at the margin of the umbilical stump.

At the time of my first examination (thirty-six hours after the circumcision was done), blood was still oozing rather freely from the circumcision wound. The patient appeared to be in good condition, but there were more of the yellowish blisters on the fingers, wrists, ankles, and toes. Some of the earlier lesions had ruptured. These and the areas on the heels had a marked resemblance to lesions one finds resulting from severe scalds.

Examination of the chest, heart, head and neck, and abdomen was negative for pathologic findings. There was no elevation of temperature.

The coagulation time was 6½ minutes, and the bleeding time was 3 minutes. The platelet count was 50,780.

The case was considered to be one of hemorrhagic disease of the newborn, with complicating pemphigus neonatorum. The child was isolated. Calcium gluconate and viosterol were given by mouth in an effort to control bleeding, and the lesions were painted with a solution of 1 per cent gentian violet. The bleeding from the circumcision stopped in about twelve hours. About this time a vesicle appeared in the soft palate. This ruptured and oozed blood for several hours.

The patient was discharged November 15. There were still several blisters over his body at this time, but there was no bleeding, and we had obtained information which convinced us that we were dealing with a hereditary skin affection rather than with an infectious disease. The family history is interesting, as shown by Fig. 1.

The patient (*A*) can trace the hereditary nature of his skin dyscrasia through his mother (*B*), his maternal grandmother (*C*), and his great-grandmother (*D*).

He has an aunt (*G*), an uncle (*E*), and a cousin (*F*) who are similarly affected. An interesting thing is that the grandmother (*C*) was one of twins. The twin sister (*H*) was not affected, and she has four children (*I, J, K, L*), none of whom are affected.

The disease, epidermolysis bullosa hereditaria, is a manifestation of a peculiar hereditary skin anomaly. There is a decrease in number of elastic fibers in the outer dermal layers and a shortening and thickening of these fibers in the deeper layers. Pressure or friction on an area of skin so affected elicits a response of bulla formation. These bullae may be filled with a yellowish transudate or may be hemorrhagic in nature. Healing may be with or without scar formation, depending upon the depth to which the skin is involved and whether or not secondary infection occurs.

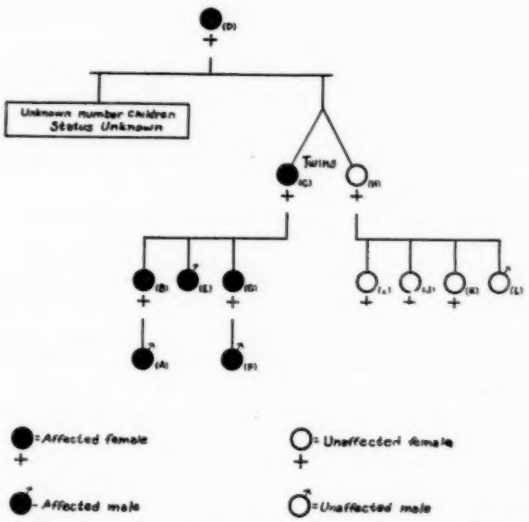

Fig. 1.—Chart showing transmission of the condition, epidermolysis bullosa hereditaria, through four generations. It also shows the absence of the condition in one of fraternal twins and her descendants.

Some writers have divided the condition into two classes, the simple and the atrophic forms. Both of these forms have been reported in the same family and probably only represent a variation in degree of absence of fibrous tissue. In the atrophic form scarring is more common, and loss of fingernails or toenails is more frequently seen. A few cases of simple bullous epidermolysis have been reported in which no family history of hereditary tendency could be obtained.

The child who is the subject of this report is now 1 year old. He is still having crops of bullae from time to time, especially during hot weather. This is said to be characteristic of the disease. He has been

rather difficult to keep free of secondary infection. The present routine is to open the bullae as soon as they appear, trim off the epidermis, and apply silver nitrate (2 per cent) to the base. Three per cent ammoniated mercury ointment is then applied regularly (*without* massage) until the area is healed. This regimen seems to be more effective than any other that has been tried. There has been some infection about the roots of several nails, which have dropped off, but these are being replaced.

All of the adult members of the family now living who have the condition are still subject to its symptoms, although some of them do not have as much trouble as others. All of them have lost fingernails or toenails on occasion, but do not report scarring as a noticeable symptom of the healing lesions. The mother experiences discomfort in wearing tight-fitting clothing, bullae forming wherever there are points of pressure.

Prognosis for the patient is good, so far as continued existence is concerned. So far as recovery from his affliction goes, however, one feels that there is no great hope. Authors have reported treatment with large doses of vitamins, calcium, thyroid, pituitary, etc., but with no success. Attempts at prevention of secondary infections of the lesions are probably all the treatment that is justified.

Probably the most important function of the physician in so far as epidermolysis bullosa hereditaria is concerned is for him to know and remember that such a condition exists. He will then inquire carefully into the family history before committing himself to a diagnosis in skin conditions characterized by bulla formation. He may thus avoid subjecting some of his patients to a vigorous routine of isolation and active therapy which is not indicated.

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HYPERSENSITIVITY TO SULFANILAMIDE FOLLOWING ROENTGEN THERAPY

M. B. Marks, M.D.
Miami Beach, Fla.

SENSITIZATION symptoms and the photodynamic responses of patients to sulfanilamide therapy following exposure to strong sunlight and ultraviolet rays have been discussed by Brusting,[1] Hallam,[2] Rogers,[3] Finney,[4] and others. Epstein,[5] experimenting on five volunteers and himself, was able to demonstrate that sulfanilamide caused definite symptoms of photosensitivity following exposure to an erythema dose of ultraviolet rays. In two of the volunteers a typical photoallergic state was reproduced following repeated ultraviolet irradiation.

REPORT OF CASES

Case 1.—*History and Examination.*—I was first called to the home of this 8-year-old white female child on March 9, 1939, to see her brother, who had injured his left ankle and subsequently developed a lymphangitis with a left inguinal adenitis. These responded nicely to hot massive compresses and sulfanilamide. The mother at that time seemed to think that the boy's infection was acquired from his sister who had been ill since Jan. 25, 1939, with a streptococcus sore throat and bilateral streptococcus otitis media. The girl was under the care of a physician all this time who had given her large doses of sulfanilamide with great improvement in her condition. At the time I saw the boy, the girl was confined to bed with a rhinitis and some residual redness in her pharynx.

On March 16, 1939, I was called to see the girl. It appeared that the mother had allowed the child up for the past two weeks, and at the end of this period a large painful swelling on the right side of her neck had developed, accompanied by high fever. She had had the swelling for the past three days and had hardly slept the previous two nights.

Physical examination at this time revealed an angry red pharynx and a right-sided upper cervical adenopathy with marked swelling and induration, and collateral edema which extended down into the back and over into the region of the anterior neck. She held her head in a fixed right position; and any slight motion caused a sharp outcry of pain. She looked toxic, and her temperature was 103.4° F. At the time there was no respiratory distress; but because of the extensive swelling and because I was fearful of an edema of the glottis, I hospitalized her.

On admission to the hospital on March 16, 1939, a blood count was done which revealed a white blood count of 22,000 with a high percentage of stabs and segmented forms. The blood picture revealed no evidences of a blood dyscrasia. The urine examination was negative as to albumin, sugar, casts, and blood. The blood culture on the following morning showed a mixed flora with a few colonies of hemolytic streptococci.

Treatment and Course.—The child was started on 7½ gr. (0.5 Gm.) of prontylin combined with 10 gr. (0.65 Gm.) of sodium bicarbonate every three hours. Shortly after her first dose of sulfanilamide, she was given an x-ray exposure of 100 roentgen units of intermediate voltage to the right cervical glandular chain. That evening the child appeared more toxic. The temperature was now 104°,

respiration 32, and pulse 144. Sulfanilamide was continued throughout the night for three more doses, and in the morning another x-ray exposure of 100 roentgen units was given. The mass in the neck now seemed even larger. The child's skin appeared tense, as if a universal subcutaneous edema were present. There was actual pitting over the sacrum and upper back. Over the entire body was a diffuse erythema; and about the upper back, sacrum, buttocks, and thighs, a typical scarlatiniform rash was present. The enlarging cervical adenitis with the concomitant edema extended forward to the anterior neck and floor of the mouth, and soon symptoms of respiratory embarrassment began. The drug was stopped immediately, and ¼ gr. (0.016 Gm.) of ephedrine hydrochloride and 15 gr. (1 Gm.) of calcium lactate were given every three hours. In the next twenty-four to thirty-six hours, the child showed marked improvement, the rash and generalized edema abating with marked regression of the adenitis. She remained in the hospital until March 20, at which time the child was allowed to go home. She was afebrile, but there was still a residual gland about the size of a walnut in the middle of the right cervical chain. The gland was stony hard in consistency but felt neither hot nor tender. She felt perfectly comfortable and was up and about.

On March 28, the roentgenologist saw her at his office and decided to give the child a small therapeutic ray to the enlarged gland in order to cause further resolution. Accordingly, a ray of 75 roentgen units was given, which caused a mild reaction over the glandular mass. Another ray of the same intensity was given on March 30, two days later. The entire right chain flared up again. The child became feverish, was unable to move her head without great pain, and the right cervical group of nodes was again hot and tender. This subsided in the next few days, and she soon was able to be out of bed. The offending gland which had formerly been so hard was now much softer and considerably smaller.

Further Course.—On April 10, I was again called to see the patient for an acute recurrence of the adenitis. The picture, however, was now different. There was a large patch of rose-red erythema covering the glandular site. The edges of the patch were elevated and sharply demarcated from the rest of the skin. Rolling the finger over the elevated edge of the lesion caused intense pain. The child appeared quite toxic. A diagnosis of erysipelas was made and the child again hospitalized.

On admission to the hospital the temperature was 103° F., respiration 28, and pulse 120. The white blood count was 17,450 with a predominance of segmented forms. There was a trace of albumin in the urine. Throat culture the next day revealed only staphylococci and nonhemolytic streptococci. Because of the former sensitization to sulfanilamide, it was decided to put the child on sulfapyridine. Fifteen grains (1 Gm.) were given initially, and 7½ gr. (0.5 Gm.) thereafter every four hours. By morning the patch appeared less angry, with a much less tender, elevated edge. The lesion had shown no signs of spread in the intervening fourteen-hour period. Her temperature had dropped to 100.2° F., and she appeared comfortable and happy. Sulfapyridine was continued, and she became afebrile. The redness disappeared, and the remaining enlarged cervical gland became very soft and boggy. It was incised on April 16, with the expulsion of much serosanguineous pus. Culture of this material revealed staphylococcic and hemolytic streptococci. On April 20, the drug was discontinued. By now all signs of the erysipelas had disappeared, and the incised area was fairly well healed.

CASE 2.—*History and Examination.*—A physician's son, aged 4 years, seen on March 5, 1939, had had, for two days, a temperature of 102.6° F., a sore throat, and swollen glands of the left side of the neck. His father stated that he had had a

similar infection ten days previously. The child, too, had recently recovered from an attack of influenza in January, 1939. Examination at this time revealed an acute tonsillitis and moderate left cervical lymphadenopathy. The child was given the usual medications but did not respond well to treatment. On March 7, the white blood count was 19,400 with a predominance of stabs and segmented forms. Urine examination was negative. Throat culture the following day revealed staphylococci and nonhemolytic streptococci.

Treatment and Course.—Sulfanilamide in adequate dosage was started, and the following day the child's tonsillitis was much improved and the temperature fell to normal. He remained on the drug for about four days. At the end of that period he was given an x-ray treatment of 75 roentgen units to the affected glands. In the morning, the glands had swelled to twice their previous size and were hot and tender. The sulfanilamide was promptly discontinued. In the next few days the adenitis had almost completely subsided. One week later the boy was taken to the beach and exposed to strong sunlight. Late that evening the cervical glands again became inflamed, although to a lesser extent than formerly. In a few days the adenitis again subsided and failed to recur even after numerous other sun exposures.

COMMENT

These cases demonstrate that x-ray treatment and sulfanilamide should not be used together, since they may produce sensitization symptoms. It seems, too, that after this sensitization occurs, a state of photoallergy may exist for a varying period. Epstein[5] has called attention to this, but further work is needed to establish whether or not this is a true allergic state. Patients who have terminated a course of sulfanilamide or its derivatives should not be given x-ray or ultraviolet exposure too soon afterward nor should they be allowed to indulge in sun bathing. This is particularly true when sensitization symptoms have occurred once before.

It is interesting to note that in the patient in Case 1, where sulfanilamide might have caused a reaction in the treatment of erysipelas, sulfapyridine was substituted with excellent results.

The following suggestions appear reasonable:

1. That the use of x-ray concurrently or shortly after sulfanilamide administration be contraindicated.

2. That, since sulfanilamide sensitizes the skin to x-ray (and some other forms of light), severe local or constitutional reactions may occur with repeated exposures even after the drug has been discontinued for some time. Caution as to successive repeated therapeutic light exposures should then be exercised.

3. That, when sensitivity to one sulfanilamide preparation exists, a change to another derivative of the drug, such as sulfapyridine, should be tried.

CONCLUSIONS

The combination of x-ray and sulfanilamide therapy may lead to unpleasant and serious side effects.

Photoallergy sometimes follows slight or moderate exposure to roentgen rays, ultraviolet rays, or even sunshine.

When sensitization occurs, substitution of one sulfanilamide derivative for another should be tried.

Sulfapyridine was used with excellent results in a case of erysipelas.

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SUBACUTE YELLOW ATROPHY OF THE LIVER

With Unusual Abdominal Venous Bruit

Harold Herman, M.D.
New York, N. Y.

ON MAY 14, 1938, a white girl, 10 years old, was admitted to the Pediatric Service of the Mount Sinai Hospital with the complaints of jaundice and enlargement of the abdomen. Upon admission, the child was in good general condition and did not appear acutely ill. The jaundice had been present for two weeks. The increasing size of the abdomen was noted one week after the onset of the jaundice. Sixteen days after her admission to the hospital, the child died following a rapidly progressive illness, with acute hepatic insufficiency and terminal pneumonia. The anatomic diagnosis at post-mortem was subacute yellow atrophy of the liver with extensive nodular regeneration.

Subacute yellow atrophy differs from the acute form in that the process may go on over a prolonged period of time, running into months or even years, as has been verified by biopsy.[1-4] Acute yellow atrophy has been defined[5] as a clinical and pathologic picture due to a variety of causes, one of which is infectious jaundice. In the rare, fatal cases of catarrhal jaundice, the picture is that of acute yellow atrophy. There is an increase in the number of atrophy cases during epidemics of catarrhal jaundice,[6] and the changes of acute yellow atrophy have been found at post-mortem in patients dying during an epidemic of acute hemorrhagic jaundice.[7] Acute yellow atrophy and catarrhal jaundice have both been attributed to infection.[8, 9] The infectious nature of yellow atrophy, however, has not been fully proved. There are certain predisposing factors which render the liver cells more prone to injury, such as (1) marked depletion in the glycogen reserve of the liver, (2) anoxemia, (3) thyroid disease, and (4) allergy.[10]

Patients with acute cases of catarrhal jaundice can recover entirely, but once the disease becomes chronic, it seems to pursue an inevitably progressive course, although the individual recurrences of symptoms may be separated by months or even years of well-being.[11] There are patients with chronic cases so insidious that the patients never show jaundice, but die of some complication of cirrhosis and the disease is recognized only at post-mortem. The association of latent liver damage with catarrhal jaundice has been pointed out by many authors.[12-14] The similarity of their pathologic pictures has been stressed.[15-18] Eppinger[16] examined histologically the livers of a number of patients with catarrhal jaundice at the height of the disease,

From the Pediatric Department of the Mount Sinai Hospital, Director, Béla Schick, M.D.

and some of them showed liver cell necrosis like that of acute yellow atrophy. There is much evidence that the jaundice is at least partly hemolytic in both. Acute and chronic interstitial hepatitis occurs in a variety of diseases without leading to cirrhosis. The old idea of cirrhosis as a chronic sclerosing interstitial hepatitis has been put in question by the tendency to regard it as a reparatory process following degeneration and necrosis of tissue. Reconstruction of the liver can occur without scarring, as, for example, in the chronic recurring forms of yellow atrophy. There are forms of this which develop into nodular hyperplasia without any cirrhosis. These are the purest forms of hepatosis. Other cases show varying degrees of hepatitis. There may be all varieties of combinations between pure hepatosis (which is rarely seen) and pure hepatitis. When hepatosis preponderates, the atrophic form results.[19]

CASE REPORT

I. H., a female of Jewish parentage, was born in 1928 in New York City. The family history is irrelevant; the mother had diabetes. The child's birth history was normal. From the ages of 11 months to 9 years, she was seen at intervals in the Mount Sinai Hospital Outpatient Department. Her physical and mental development were normal. She was always underweight and somewhat undersized for her age. She never ate well. She was treated as a case of "malnutrition," but the physical examinations revealed no abnormalities. The liver was never reported to be enlarged. Her past history included immunization against diphtheria and smallpox, purulent otitis, tonsillitis, cervical adenitis, measles, pertussis, grippe, operation for "acute appendicitis," and tonsil and adenoid removal. At 9 years of age, she suffered an attack of abdominal pain, for which she was seen only once in the Outpatient Department.

Because of poor home conditions, she was placed in an orphanage in September, 1937, and remained there up to the time of her admission to the hospital. All physical findings and laboratory tests and immune reactions performed while at the orphanage were normal. Her health seemed good. She had no complaints and attended school without a single day's absence until the onset of her terminal illness in May, 1938. On April 10, 1938, a complete semiannual examination revealed no abnormalities, and her health and progress seemed satisfactory.

On May 1, three weeks later, the child was brought into the infirmary because of jaundice. There was no evidence of infection. The liver was not palpable. There was no discomfort or pain, nor were there gastrointestinal symptoms. The urine showed no bile at this time; albumin was negative; a trace of sugar was present. The stool was somewhat light in color. During the next week, there was progressive increase in the jaundice; the stools became acholic, and the urine contained bile and traces of sugar. The patient was quite comfortable. Her abdomen, however, had enlarged, and her weight had begun to increase. By May 14, the case had progressed further. The abdomen had enlarged two inches; the weight had increased by 3½ pounds; the urine was deeply bile-stained; the stools were clay-colored; the jaundice was more intense and in the last twenty-four hours, she had had two mild nosebleeds. She was referred to Mount Sinai Hospital where she was admitted with the diagnosis of "jaundice, probably of an obstructive nature."

Physical examination on admission revealed a fairly well-nourished and well-developed white female, intelligent, rational, cooperative, and not acutely ill.

The temperature, pulse, and respiration were normal. The skin was deeply icteric; there was no eruption or itching. The abdomen was markedly distended and seemed to contain free fluid. No masses were palpable. Over both sides of the abdomen, extending from the crest of the ileum upward to the lower part of the chest, were several dilated veins. Auscultation over the xiphoid process revealed a constant bruit, which became louder on inspiration or when pressure was placed upon the abdomen. The bruit was loud and continuous, occasionally sounding like a waterfall or a wind blowing through a cave, and sometimes it had a whistling note. It was diminished somewhat when the child was in the upright position. This bruit was transmitted over the lower part of the chest on both sides to the anterior axillary line and over the upper part of the epigastrium. Rectal examination was negative. The blood pressure on both arms was 104/64, and over the legs, 140/90. The chest was clear. Neurologic examination was negative. An x-ray examination of the abdomen showed distention of the stomach and of the bowel, but no other abnormalities were demonstrated. No evidences of varices of the esophagus were found. The stools were light brown, showed a 2-plus guaiac, were positive for urobilin, and negative for bile and parasites. The urine contained bile and urobilin, but was otherwise negative. A galactose tolerance test was done, and 12 Gm. were excreted. The saccharine time was 8 seconds.

During the first few days after admission, several telangiectasia and spider-web hemangiomas made their appearance on the cheeks and over the body.

Sound tracings on May 17 revealed the bruit to be synchronous with radial pulse, cardiac impulse, and jugular pulse tracings. The bruit was unchanged by the removal of air from the stomach. Two days later its character changed. It had developed a to-and-fro component with a high-pitched whistling quality. It could now be eliminated by pressure of the stethoscope in listening to it.

The patient's stools varied in their content of bile and urobilin. Up to the day of admission, they had been quite clay-colored, but shortly thereafter, bile again appeared in them. Duodenal drainage was done and revealed normal A and B bile. The van den Bergh direct test was promptly positive; blood bilirubin was 8; nitrogen was 7; cholesterol was 165, with only a trace of ester; phosphorus was 4.5; calcium was 10.2; and the icteric index was 38. The Janney test showed no sugar in the urine. The fasting blood sugar was 65 mg. per cent; at one-half hour, it was 135; at one hour and fifteen minutes, 185; and at two and one-half hours, 110. The blood Wassermann test was negative. A check-up of the cholesterol on May 20 showed a total cholesterol of 145, with only a trace of ester; the blood urea nitrogen was 9, and the icteric index was 42.

When it was found, on May 20, that the jaundice was growing deeper and the child was becoming dehydrated and drowsy, hypertonic glucose was given intravenously. Fever was now present. Abdominal paracentesis was done on May 21 and yielded 30 c.c. of slightly turbid, yellow fluid. The specific gravity of the fluid was 1.012; it contained 5,500 white blood cells, with 95 per cent polymorphonuclear and 5 per cent mononuclear cells; no organisms were found in the smear nor on the culture; no tumor cells were found; the protein content was 0.4; the Takata-Ara test was strongly positive.

On May 23, the icteric index had gone up to 60, the blood sugar was 80, and the urea was 10. A Takata-Ara test was positive. Total proteins were 5.3 on May 25. Albumin was 2.9, and globulin was 2.4. Examination of the urine for tyrosine was positive on one test, but negative on two other occasions.

The blood counts were irrelevant save for a secondary anemia with the white cells ranging from 11,000 to 16,000 with polymorphonuclears from 50 to 64 per cent and large mononuclears increasing to 11 per cent. The platelets were low, and occasional reticulocytes were seen. The bleeding time was 7 minutes. The tourniquet test was negative. Clot retraction was sluggish (4½ hours). The

coagulation time was 3½ minutes. A fragility test showed no hemolysis at 0.72, partial at 0.45, and complete at 0.24. The volume of packed red blood cells was 41.42, and the mean diameter of the red blood cells was 86.3

The temperature, which had been 100° F. on admission, remained at about that level until May 21, when it rose to 102.8° F. and fluctuated just about at that height until the terminal state, when it rose to 106° before exitus. On about the seventh day of hospitalization, the child began to grow drowsy, and from that day on, her course was progressively downhill. Jaundice deepened, turgor became poor, and she became irrational and disoriented, and all of this despite frequent infusions of hypertonic glucose and several blood transfusions. On May 29, respirations became Cheyne-Stokes in character. The patient became deeply comatose and gradually weaker. The chest filled up with moisture, and she died on May 30, with the presence of cholemia. An autopsy was performed, and the reported cause of death was hepatic insufficiency and bronchopneumonia. The anatomic diagnosis was subacute yellow atrophy of the liver with extensive nodular regeneration.

Post-Mortem Examination (Performed by Dr. A. Pollack).—A summary of the anatomic findings follows:

Subacute yellow atrophy of the liver with extensive nodular regeneration; jaundice; ascites; prominent collateral portal circulation; wide paraumbilical; esophageal, coronary, and diaphragmatic veins; splenomegaly; accessory spleen; congenital dystopia of kidneys; status post appendectomy; parenchymatous degeneration of heart and kidneys; petechial hemorrhages of mitral valve leaflets; patent foramen ovale; hemorrhagic bronchopneumonia of the lower lobes; lobular atelectasis of all lobes; pulmonary congestion and edema.

The relevant details of the autopsy are as follows:

The *liver* was approximately half the normal size. It weighed 420 Gm. The shape was bizarre because of the atrophy of some portions and irregular hyperplasia of others. The superior surface of the right lobe was for the most part, smooth and reddish in color. It was studded by several nodules from about 1 to 1.5 cm. in diameter, yellowish in color, and raised above the surface as much as a centimeter. The lateral border contained several yellow nodules as large as a walnut. The posterior aspect was composed of a fusion of several irregular yellow bosses. The left lobe was remarkably thinned. There was actually very little liver tissue to the left of the falciform ligament, except for several hyperplastic areas to the left of the inferior vena cava posteriorly. The smooth appearance of the greater portion of the right lobe belied its true condition, for, on section, the bulk of the lobe was found to be made up of a large, bulging, yellowish, tumorlike, hyperplastic mass about the size of an orange. This came to within a centimeter of the superior surface. It was in striking contrast with the appearance of the narrow cortical strip, which was dark red, fleshy, firm, and flat on cut section. It had the appearance of splenic tissue. No liver lobule architecture could be seen in this red area. The yellow area, on the other hand, bulged strikingly after section and appeared very cellular. Here also, however, no lobular architecture could be distinguished. The extreme lateral portion of this lobe contained several small round nodular areas which had a mixed yellowish and hemorrhagic appearance. Other areas in this portion of the liver showed a distinct grayish-red network dividing off nodules of irregular outline and varying size. A similar thing was found in the left lobe in those red areas which were apparently atrophic. There was not yet retraction of these grayish-red streaks from the cut surface.

The portal veins were not changed. The left branch was of normal size and hence appeared large in relation to the atrophic lobe which it supplied. The

umbilical vein was open as far as the anterior edge of the liver where it ended blindly in the ligamentum teres. It communicated laterally, however, with a large venous sinus which had numerous tributaries from the liver. This sinus was continuous with dilated thin-walled paraumbilical veins which traversed the falciform ligament and were traced to the subcutaneous tissue around the umbilicus. The main hepatic ducts and gall bladder and blood vessels were unchanged.

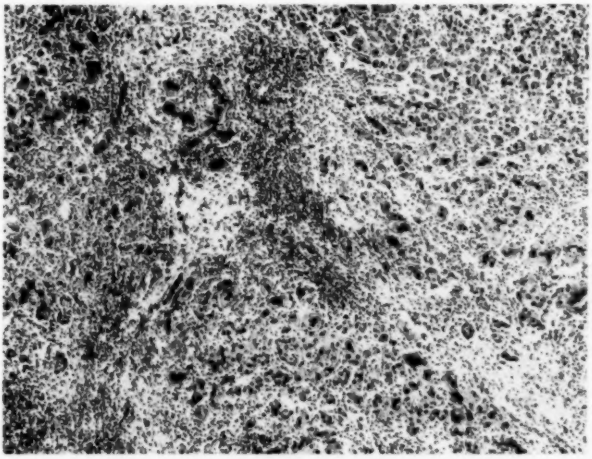

Fig. 1.

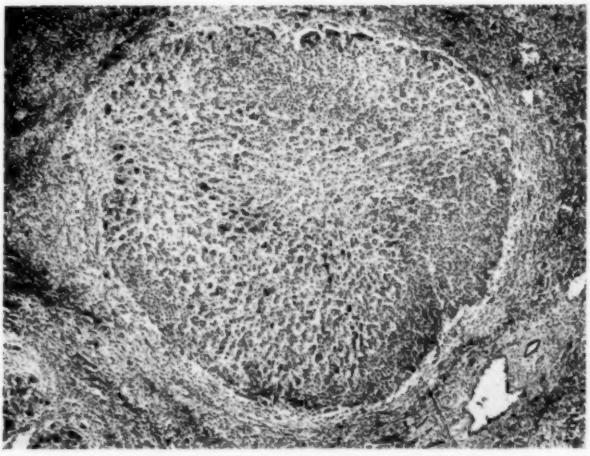

Fig. 2.

Microscopic Examination.—Sections taken through areas of red atrophy or "splenization" showed an almost complete absence of polygonal cells (Figs. 1 and 2). They were composed of a meshwork of engorged sinusoids interspersed with nests and strands of "bile-duct sprouts," the whole representing a collapse of the mesenchymal component. Here and there in these atrophic portions one

found small islands of regenerating polygonal cells, some of which were undergoing secondary degeneration. Reactive acute inflammation was present, with leucocytes, plasma cells, and eosinophiles.

Those areas, which presented grossly as large yellow nodules, appeared microscopically as smaller and larger pseudolobules of regenerating liver parenchyma. There was no orientation resembling the normal lobule. The regenerating cells formed irregular cords separated from each other by sinusoids. Somewhere the cords were broken up. An argentaffin fibrilloid skeleton bore the same relation to these regenerated cords as did that of the normal liver, except that the liver fibers appeared heavier. The polygonal cells were large and irregular. Many were multinucleated and atypical, particularly at the periphery of the pseudolobules, where, also, the new liver cells often anastomosed with "bile-duct sprouts" which were found in the atrophic meshwork. In the latter areas, obliteration of the sinusoids and further contraction led to fairly wide bands of fibrous tissue, which included larger vessels, larger bile ducts, and "bile-duct sprouts." The subcapsular zones showed this contrast most strikingly.

The *spleen* weighed 280 Gm. and was enlarged and a little flabby. Microscopically it was extremely hyperemic. Follicles were numerous but small, and without secondary centers. Pulp cords were very rich in reticulum cells. In some areas, the pulp cords were engorged, while adjacent sinusoids were relatively empty. There were numerous foci of myelopoiesis.

The *bone marrow* was red and spongy. Microscopic examination showed marked reduction in megakaryocytes, but otherwise, active hematopoiesis.

DISCUSSION

The etiological factor or factors in this case cannot be named. The time of onset or total duration of the condition cannot be determined. Surmise might direct suspicion to the attack of abdominal pain in 1937 or to the "acute appendicitis" of 1935. The patient was never reported to have jaundice or an enlargement of the liver or spleen. There is no history of chronic indigestion. She received a general ether anesthesia twice, but seemed to suffer no ill effects afterward.

When admitted to the hospital, she did not seem seriously ill. She was quite comfortable and not at all toxic. The diagnosis of obstruction seemed to be the most probable one.

However, it was soon realized that the liver was severely damaged, because the cholesterol was not high and the ester fraction was present only in traces. The markedly positive galactose test, the presence of tyrosine, and the positive Takata-Ara test reaction also substantiated this conclusion. The fluctuation in the amount of urobilin and bile in the stools, with the presence of normal A and B bile, ruled out obstruction.[20-23]

The *bruit* is an exceedingly interesting phenomenon which is not diagnostic of the type of lesion in the liver. It was first described in 1883.[24] Since then much has been written about it under the names of venous bruit, hum, or epigastric murmur.[25-35] The descriptions all resemble each other fairly closely, and our case is no exception. Minor variations have been reported, one such being an occasional accompanying thrill.

The closest approach to a vivid description is the "roaring of a wind through a cave" or "the humming of a top."[28] The hum is louder on inspiration, and it may diminish or disappear spontaneously or as the result of tapping, although this is not always the case. There is no relationship to anemia. Postural variations and changes following the application of external pressure have been noted. Sometimes it has been heard best near the umbilicus.

The most commonly accepted theory today is that it is caused by the passage of blood through a constricted lumen into a relatively dilated channel, in much the same way that the bruit de diable is thought to be caused by the blood flowing in the jugular veins and suddenly coming through the deep cervical fascia. Thus, a constriction of the inferior vena cava in its passage through the liver would give rise to a venous hum where it pierces the diaphragm. The sudden entrance of blood from any small channel into a larger channel, and vice versa, should give rise to this sign. This has been verified by post-mortem studies. A bruit has been found associated with the dilatation of an incompletely obliterated umbilical vein,[29] and again with a thin-walled vein as large as the little finger, running in the falciform ligament, in a case of cirrhosis.[36] The regional pathology in the case here reported fits very closely into this category.

SUMMARY

A case of subacute yellow atrophy of the liver with autopsy findings is reported in a female child, aged 10 years. The laboratory examinations suggested the correct diagnosis during life.

The entire duration of the condition could not be determined from a careful study of the past history. The terminal illness lasted approximately four weeks. The presence of a venous bruit, with a study of the accompanying regional pathology, was of particular interest.

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27 West Ninety-Sixth Street

Special Article

JEALOUSY

DAVID M. LEVY, M.D.
NEW YORK, N. Y.

IN THIS article I am using the word "jealousy" to include the word "envy." As far as the study of the jealousy of the child within a family is concerned, the word rivalry is probably more descriptive, including as it does all the activities of a child in relation to a brother or sister, motivated originally by jealousy. A child may be jealous in that he wants his mother to pay attention to him alone, or more attention to him than to the baby. He may be envious of a brother's gift, of his good work in school, or of the praise he receives. In these respects, his envy is based primarily on jealousy, since he is jealous of the love and recognition that are turned away from him to another.

In young children of the same family, their jealousy is largely a derivative of the relationship to the mother. Most of the problems of rivalry among brothers and sisters are based on jealousy of the mother's love.

It is not difficult to understand the tremendous energy in the child that arises from this source. It is best demonstrated in the case of the first-born child of an indulgent, loving mother. Consider such a child at 3 years of age. Practically his entire social and emotional life is invested in the relation with the mother. He has been loved, cherished, admired, and indulged by her. All his wants have been satisfied within this relationship, which may be likened to the atmosphere he breathes. Now let us suppose at this age a second child arrives who becomes the object of the mother's devotion. The dislocation in the life of a 3-year-old can now be clearly envisaged, since his life was entirely involved with his mother. His reaction of fury against the newcomer is as patent a process as the struggle for air when a person is asphyxiated. The reaction of the displaced child whose world has been shattered by the new event will, in the case mentioned, be a furious assault upon the baby. Hatred is unleashed, first against the baby, then against the mother, who has really dethroned her first infant in more brutal a manner than she realizes. Since the child's aggression against both mother and baby is more or less futile, he then resorts to displays of anger, demands for attention, and various symptoms in which he goes back to an earlier way of

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behavior, acting more like a baby than he is, as though in this way to win again the paradise he lost. This last maneuver is known as regression.

The example given may be considered extreme because of the assumption that the 3-year-old who was so adversely affected by the baby's advent lived a life exclusively in relation to the mother. However, the picture given is merely a full display of the activities that transpire, more or less, in every instance where the child must adjust to the problem of the new rival.

A number of studies have shown actually that the difficulty engendered in the older child is in direct proportion to the strength of the maternal bond. In other words, the closer a child is to his mother the more he has to lose when she turns away from him. That is how we explain the fact that in groups of children the larger the age difference between a child and the next younger, the less is jealousy manifested. Imagine a family of two children in which the older is 12 when the baby is born. In that case there can be no comparison in seriousness with the situation of the 3-year-old that was described. The 12-year-old has numerous relationships—father, friends, teacher—and various interests and activities. The 12-year-old is, in general, relatively independent as compared with the indulged, overprotected 3-year-old. However, if the 12-year-old has remained in a highly overprotected state, then the reaction to the baby can be quite similar to the behavior of the 3-year-old.

There seems to be some evidence, also, that where the age difference of the older and younger is very small, say not more than one year, or practically does not exist, as in the case of twins, there is also distinctly less manifestation of jealousy. In such instances, one may say that the child arrives in a world of three rather than a world of two, and has made a natural adjustment.

In any family, problems of jealousy arise which are so frequent as to be considered perfectly normal. The commonest is jealousy regarding the privilege of the older to go to bed at a later hour. The younger child who gets the altered, discarded clothing of the older is another case in point. Since parents are human beings and respond differently to their different children, there is a high degree of alertness on the part of the recipients of their attention. If the differences are great, a struggle for affection and recognition ensues on the part of the unfavored. This struggle makes the unfavored rather obnoxious and thereby gives the parent a feeling of increased justification in favoring one child over another. As the dispensers of good things, parents should be aware of the fact that the child's fault may have originally been in demanding recognition that was withheld.

A child's jealousy of the mother may be quite like the jealousy of a lover. When extreme, both give evidence of great insecurity when

not fully in possession of the beloved object. The adult variety, indeed, may be derived from the original relationship to the mother. Everyone seems to be aware of one or more instances in which the lover is jealous of every movement, every expression, and wants to compel exclusive devotion. He (or she) finds a cause for quarreling in the slightest glance or smile bestowed on another. The jealousy involves even the necessary occupation of the loved one. The relationship becomes quite a tyrannical one, and commonly ends in disaster, because the limit to endurance of the jealous and possessive person is bound to be reached. So it is with the child who refuses to let the mother go out, to talk with anyone but himself, who makes the mother his slave, who develops various symptoms and anxieties all designed to keep the mother constantly at his side.

How can the mother avoid the possibility of being enslaved? How can she avoid, at least, excessive display of jealousy among her children? It is easy to give advice on such matters. The ability to use it will depend more on the mother's personality than on her intellectual capacity or intentions. If the mother sacrifices everything for the child, she is often remarkably immune to warnings of danger that the child will become a totally dependent being. When a point arrives at which she becomes the victim of tyranny to such a degree that she cries out for help, then something may be done. In general, the mother who has a natural love for her child and gives him free and frequent social contacts with other children and adults during his second and third year of life is playing pretty safe. Further, if the child develops such resources that he can amuse himself for periods of time without requiring the constant presence of his mother as the audience, he has an important advantage in life.

When two children of the same family are playing together pleasantly and trouble arises as soon as the third one appears, the chances are great that we have a problem in jealousy arising out of the maternal relationship. Awareness of the discordant note and the early use of the child guidance clinic are great aids. However, the mother alone must be the judge of how discordant the note is, because there are many problems that can be solved within the family and quite a number that somehow seem to solve themselves. But certainly it is not difficult to know that it is a problem that has gone beyond the area of the family's own attempts at solution when it happens that every time little John enters the house there is bound to be trouble.

Up to this point I have dwelt on the difficulties that arise from the attitude of jealousy. It is only fair to show the other side—to show its constructive features. Jealousy is the cause of competition among brothers and sisters and hence a fertile source of energy. In attempting to outdo each other, children put forth greater effort, an effort to

attain recognition within the family that stimulates development in intellectual and social life. The children try to outdo each other at sports, in school work, in making clever remarks, in handicrafts, in manners, and in neatness. One child is scolded for being sloppy; the other immediately displays his neatness. Of course, this can all go too far, but within limits such competition may have tremendous value, and surely the history of the development of numerous talents has been made on this basis.

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Critical Review

EXPERIMENTAL POLIOMYELITIS IN ANIMALS OTHER THAN THE MONKEY

A Review of the Literature*

John A. Toomey, M.D.
Cleveland, Ohio

REPEATED attempts have been made to produce poliomyelitis in smaller laboratory animals. The reasons are obvious. Could the disease be consistently given to smaller animals, the cost of experimentation would be at least 75 per cent less than it is now; a great amount of fundamental work could be attempted, and more workers could afford to interest themselves in this problem.

Flexner and Lewis[1, 2] injected virus into a number of rabbits and guinea pigs, one horse, two calves, three goats, three pigs, three sheep, six rats, six mice, six dogs, and four cats. Although the animals were under observation for many weeks, they did not develop any appreciable symptoms of the disease. Flexner[3] thought that poliomyelitis might be produced in poultry, dogs, and, possibly, horses. He later made repeated attempts to transfer the disease to these animals without success.

Krause and Meinicke,[4] as well as Lentz and Huntemüller,[5] inoculated rabbits with cerebrospinal fluid, blood, brain, and spleen obtained from human beings who were ill with poliomyelitis or who had died from the disease. The animals died, and similar tissues from their organs were inoculated into other rabbits which also died. They obtained their best results when they injected the inoculum either intravenously or intraperitoneally. Similar results were obtained when emulsions or Berkefeld filtrates of the organs mentioned were injected. Sixteen rabbits were injected in their first experiment.[4] Death occurred in from seven to eleven days, no previous objective signs having occurred. Seventeen rabbits, varying in weight from 450 to 1,250 Gm., were then inoculated either intravenously or intraperitoneally with infected poliomyelitis monkey cord filtrate in doses ranging from 5 to 20 c.c. Five days later one animal, which had received a dose of 20 c.c. intraperitoneally, suddenly developed generalized convulsive seizures and general motor weakness and died within an hour. The post-mortem examination was negative.

In the experiments of Marks,[6] young rabbits weighing from 350 to 550 Gm. were used. A 12½ per cent saline suspension of brain and spinal cord obtained from a poliomyelitis-infected monkey was thoroughly mixed, shaken mechanically, centrifuged, and the supernate passed through a Berkefeld filter. From 2.5 to 35 c.c. of this filtrate were injected either intravenously or intraperitoneally. In serial experiments from rabbit to rabbit, the animals were usually inoculated

From the Department of Pediatrics, Western Reserve University, and the Department of Contagious Diseases, City Hospital, Cleveland.

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with filtrates and emulsions made from the brain and cord, but occasionally the spleen, the liver, or defibrinated blood was used. The brain and cord of the animals of the second succeeding series were ground in 80 c.c. of saline solution and treated as were the monkey tissues; the spleen and liver were made into emulsions. There were no reactions until about eight to fifteen days following the injections, when general tonic and paroxysmal convulsions, rigidity, and opisthotonos appeared with or without clonus. The animals were weak in the interim between convulsive seizures and usually died the same day, often within from ten to thirty minutes after the first seizure. Postmortem examination showed hyperemia of the central nervous system. Marks believed that filtrates prepared from the nervous tissues of monkeys infected with experimental poliomyelitis were not wholly innocuous to young rabbits, since filtrates and emulsions made from the organs, etc., of these animals were capable of producing identical results in other rabbits as far as the sixth series. He made three successful transfers of the disease from rabbits to monkeys, one each from the second, fourth, and sixth passages. The filtrates injected were made from the brain and spinal cord of rabbits and were prepared in the manner described.

Marks' experiments seem clear-cut, but they should be confirmed in view of the universal failure to produce poliomyelitis in rabbits. If his results were true, it would have to be admitted that the virus of poliomyelitis could be propagated in individual rabbits, at least through a limited series of inoculations. It was not shown whether the virus demonstrated to be present actually multiplied in the animal or was merely mechanically present, i.e., a residuum of the inoculum. However, the virus was found in other organs, especially in the liver and spleen, as well as in the brain and cord. Whether or not smaller animals are reservoirs of infections has never been proved.

The experiments of Krause and Meinicke[4] were indefinite. They neither reproduced anything resembling the clinical disease in rabbits nor ruled out the mechanical effects that might have been produced by various methods of injection.

Neustaedter[7] stated that Römer had observed that guinea pigs frequently died of a paralysis similar to that of poliomyelitis, a paralysis which he later found to be due to a nonbacterial filtrable virus. This disease could easily be transmitted from one guinea pig to another. The virus had an incubation period of from nine to twelve days, and it caused a flaccid paralysis, usually of the hind legs with involvement of the urinary bladder. Microscopically, the pathologic picture in the cord resembled that seen in the cord obtained from a human being who had died of poliomyelitis. One of Neustaedter's monkeys, injected with an exceptionally virulent emulsion of poliomyelitis-infected cord, was placed in a cage with a wire bottom, underneath which were some guinea pigs. The monkey developed poliomyelitis four days later, and its cord showed typical lesions characteristic of poliomyelitis. The day following, two guinea pigs had paralyses of the hind legs and died that night. One was destroyed. In the cord of the other, there were foci, a diffuse distribution of mononuclear cells, a perivascular infiltration of the same cells in the pia of the anterior longitudinal fissure, marked neurophagocytosis, and numerous hemorrhages in the gray matter. The ganglion cells were so degenerated as to be hardly discernible. An emulsion of the cord of this animal was rubbed onto the

nasal mucosa of another guinea pig, and six days later it died during a convulsive seizure. At autopsy no pus was present, but there was edema of the cord and the brain. Histologic examination showed vascular infiltration of round cells, marked hemorrhages in the gray matter, slight neurophagocytosis, and marked degeneration of the ganglion cells of the anterior horns, as well as some infiltration of round cells in the pia around the olfactory bulb, etc.

A smear made from the nasal mucosa of this animal was rubbed on the nasal mucosa of another guinea pig. The latter was found dead on the seventh day. Histologic examination of the cord showed perivascular infiltration of round, dark-staining cells in the white substance of some sections (especially about the anterior horns in the lumbar sections), marked diffuse round cell infiltration in the gray substance, minute hemorrhages, and complete degeneration of the ganglion cells. The filtered virus obtained from a poliomyelitis-infected monkey cord was swabbed over the nasal mucosa of another guinea pig which developed paresis of the left leg two days later. At autopsy, it was found that there was perivascular and pericellular infiltration of leucocytes, a condition especially marked about the anterior horns of the gray matter of the lumbar area. Neustaedter, like Römer, assumed that the first two and the sixth guinea pigs of the series presented the clinical symptoms and the pathologic lesions of poliomyelitis. The first guinea pig was probably infected when virus from the infected monkey dropped through the screen and became mixed with the dust of the cage in which the former lived. Such experiments seem most interesting, but they are insignificant unless the infection is successfully transferred to monkeys for more than one generation. Even then, in these days of multiplicity of spontaneous and induced virus infections in laboratory animals, it would first have to be proved that the virus in question was poliomyelitis virus.

A most interesting set of experiments was done by Rosenau and Havens.[8] Using the Amoss strain of virus, they obtained positive results in young rabbits under six weeks of age and succeeded in transferring the virus from rabbit to rabbit through eight successive generations. They injected the virus in various ways, intracerebrally, intravenously, by nasal infiltration, and by injection into the sciatic nerve sheath. Positive results were obtained in twenty-two of fifty-four rabbits inoculated. The incubation period in these twenty-two rabbits varied; the shortest was two, and the longest was forty-one days, the average being twelve days. The incubation periods of two and forty-one days occurred after intracerebral injections.

The doses injected and routes were: 1 c.c., intravenously; 0.5 c.c., intracerebrally; 1 c.c., intranasally; and 0.5 c.c., into the nerve. The symptoms varied. Two syndromes were recognized, one of which was *progressive* in type. The rabbit became inactive, lost weight, and appeared to be weak. This was followed by partial or complete paralysis of one or more of the extremities, a condition which progressed until death. The duration of the disease varied from one to two days to one week. The paralysis was usually flaccid, but occasionally it was spastic. The other syndrome was a *fulminating* one and explosive in character, developing suddenly and terminating in a very short time. Its duration was usually only a few hours, but never more than two days. The outstanding symptoms were extreme weakness and marked dyspnea. When symptoms lasted for more than two or three days, loss of weight

was the first observed sign. The period of incubation was as variable in the eighth as in the first series of animals injected. The virus did not irritate the nerves when it was injected into their sheaths, and there was no evidence of its becoming either adaptable or fixed.

On gross examination, there was injection of the vessels of the pia, hyperemia of the gray matter of the medulla and cord, and edema throughout the brain and cord. In the progressive type of syndrome, the microscopic lesions were distributed rather uniformly throughout the gray matter of the cord and medulla. In the fulminating group, the lesions were more marked in the medullary areas of those rabbits which exhibited symptoms of respiratory failure without paralysis of the skeletal muscles. On microscopic examination, lesions consisted of capillary congestion, focal hemorrhages into the gray matter, degeneration of the large motor cells, and infiltration with cells of uncertain origin. The latter seemed to be chiefly proliferated glia cells, unlike the infiltrating lymphocytes seen in the lesions of human poliomyelitis. It cannot be stated whether or not specificity was present in these experiments, since no attempts were made to transfer the disease to monkeys.

Mathers[9] examined fresh material obtained from ten cases of poliomyelitis and found a peculiar polymorphic streptococcus type of organism in nine instances, seven of which were pure growths. Similar organisms were demonstrated microscopically in the tissues of the central nervous system. Cultures made from this organism were injected into young rabbits, and paralysis of various groups of muscles and characteristic lesions in the central nervous system, such as hyperemia, edema of the tissues with hemorrhages, round cell perivascular infiltration, and neurophagocytosis in the spinal cord, especially in the gray substance, were produced. These reactions were similar in every detail to those characteristic of acute poliomyelitis in man. Eighteen rabbits were inoculated with these streptococcus-like organisms obtained from the brain and cord of a fatal case of poliomyelitis. In from three to seven days, ten developed definite paralysis of one or more groups of muscles. In fifteen autopsied animals, there were marked changes similar to those found in acute human poliomyelitis. The first six rabbits were injected intravenously with the washed sediment of from 6 to 8 c.c. of the original ascites or dextrose broth cultures of the spinal fluid. A second series of small rabbits was inoculated intravenously with twenty-four-hour ascites dextrose broth cultures of these organisms obtained from single colonies grown on blood agar plates. Examination under low power showed round cell infiltration in the gray substance of the spinal cord of the dead animals, a condition similar to that seen in human beings who died of poliomyelitis. Subsequently, Rosenow[10a, b] and Cooper[11] revived interest in the streptococcus as a causative factor. The one objection to all such experiments has been that cross-neutralization has never been shown.

Smillie[12] found that monkeys inoculated with cultures of Flexner's globoid bodies did not get the disease. He stated that the ultimate criteria of experimental poliomyelitis consisted in (1) typical histologic lesions and (2) recommunicability of the disease by inoculation of the nervous tissue in a second animal.

Tsen[13] tried to immunize rabbits against poliomyelitis by injecting the virus. Two fruitless experiments were done, and he concluded that they could not be immunized with poliomyelitis virus to the point where they would produce a neutralizing antiserum.

Amoss[14] injected streptococcus filtrate, etc., into rabbits, and even though the agglutination titer of the blood serum reached 1:4,000 against the streptococci, it did not neutralize poliomyelitis virus. Monkeys which had been injected previously with streptococcus did not develop protection against subsequent injections of poliomyelitis virus.

Amoss also injected rabbits intracerebrally with about 0.5 c.c. of virus and, after certain intervals, killed the animals, dissected out the area at the site of the injection, and reinjected a ground suspension of this into monkeys. The only monkey that developed paralysis was one which had received an emulsion from rabbits that had received poliomyelitis virus intracerebrally four days previously. He concluded that injections of poliomyelitis virus did not bring about any symptoms in rabbits, provided the volume of the injection was not sufficient to cause dangerous intracranial pressure. Other than pressure effects, no symptoms were noted. He concluded that poliomyelitis virus may survive in the brains of rabbits for about four days as determined by tests in the monkey, but that it cannot be detected after seven days. (It is to be noted here that in all of his experiments he used the cerebral site of injection and did not use rabbit cords. These experiments could be considered negative, since the survival of the virus does not signify multiplication.)

Stimson[15] performed an experiment with four groups of six rabbits each. All but four animals were given monkey brain and cord emulsion; the latter four received saliva. The injections were made intracerebrally, intraperitoneally, or intravenously, and sometimes one animal was given two kinds of injections. Saliva was always inoculated intraperitoneally. The animals died within one day to two months after injection. Subinoculations were made into other animals, with negative results. Eight rabbits were inoculated intravenously with from 1.5 to 5 c.c. of brain cord emulsions filtered through a Berkefeld N. Ten days later another dose was given, but the animals did not develop any symptoms. In another experiment, he had four groups of six guinea pigs each to which he gave similar injections, including saliva intraperitoneally, and no disease was produced. In the third experiment there were three groups of six rabbits each to which he gave the same type of injections, including saliva intraperitoneally. He even made subinoculations in other animals, and although the injections were always followed by a high mortality in from three to sixteen days, paralysis was not produced and no virucidal serum was demonstrated in the blood sera of the injected animals.

Nevin and Bittman[16] stated that the results are variable when young rabbits are used and that the symptoms they evidence are different from those observed in monkeys and in man. They used a 5 per cent unfiltered suspension of poliomyelitis virus which was inoculated intracerebrally, intraperitoneally, or intravenously into 6-week-old rabbits. The intracerebral route was most frequently employed. Ten rabbits were injected intracerebrally with from 0.25 to 2 c.c. of material, control monkeys being injected at the same time. In all, five passages were tried. In only two rabbits did symptoms of poliomyelitis occur that were at all comparable to those seen in the monkey or in man, or that corresponded to those symptoms described by Rosenau and Havens[8] in the "progressive paralytic" type of syndrome. One rabbit had weakness of the posterior extremities, the legs being held wide apart. After the third subpassage, another developed similar symptoms on the

fourteenth day. Of the remaining twenty-six rabbits which succumbed, five died within twenty-four hours. It was impossible to determine the cause of death of the twenty-one rabbits which survived longer than twenty-four hours and which lived, in some cases, as long as a month following the injection. A large number of the animals died after varying periods of incubation, without having shown characteristic symptoms of poliomyelitis. The factor of infection was carefully controlled by cultures. The possibility of anaphylactic shock due to a foreign protein was considered, and a series of young rabbits was inoculated with normal rabbit brain suspension. The results were essentially negative.

Fairbrother[17] used 4- to 6-week-old rabbits varying in weight from 400 to 650 Gm. He inoculated them intracerebrally, intravenously, and intraperitoneally with combinations of 5 per cent emulsions of cord virus. A few were given 10 or 25 per cent suspensions. Of the eighteen injected intracerebrally, six died; of the three injected intravenously, none died; of the two injected intraperitoneally, none died; and the one injected intracerebrally and intraperitoneally did not die. Four of the six animals that succumbed died within twenty-four hours after the operation, probably from any one of the following: shock, hemorrhage, the anesthetic, the operation, etc. One died on the seventh, and the other on the seventeenth, day. The pathologic examination of the former was negative. Subsequent intracerebral transfers of its cord into three other animals gave negative results. Repeated intracerebral inoculation on fourteen occasions at later dates gave negative results. He tried a human strain in six animals, injecting four intracerebrally, and two, intracerebrally and intraperitoneally. The results were negative.

He tried to accommodate the strain in subsequent experiments and inoculated six treated animals. In twenty-four hours, the area about the inoculation was excised, ground in saline, and injected into three monkeys. The virus was present for four days about the site of injection after intracerebral inoculation. His other experiments were negative, and he concluded that rabbits were of no value in the study of poliomyelitis.

Thompson[18] tried to infect by the testicular route. He thought that he might adapt poliomyelitis virus to the rabbit. The apparent symbiosis of vaccinia and poliomyelitis virus in the monkey's skin reported by Thompson suggested an additional way to aid adaptation. He used rabbits weighing from 1,500 to 2,000 Gm., save in one series of experiments where very young animals were used. The virus was a 20 per cent Aycock strain, and the vaccine virus was a 20 per cent centrifugalized suspension of a four-day growth of a Noguchi testicular virus. First he tried to produce poliomyelitis by injecting the virus directly into the testicle. Later, he injected mixtures of equal parts of poliomyelitis and vaccine virus. One cubic centimeter of the poliomyelitis virus suspension was injected into each testicle of ten rabbits. The testicles of eight were later removed at periods varying from one to seven days after the injection. There was only a moderate local inflammatory reaction. Symptoms occurred in only one animal, which had a paralysis of the forelegs on the seventh day. The cord of this animal showed only patches of round cell infiltration which were present in the cords of control animals. Three rabbits were injected with a combination of poliomyelitis and vaccinia virus, but they developed only vaccinal reactions.

Serial passage injections of virus were then made testicularly in several rabbits at four-day intervals, the final passage injection being into the brain. Twenty per cent testicular emulsions were reinjected into the testicle of the new animals. The testicular emulsion of the fourth animal was injected into the fourth ventricle of the fifth animal. No symptoms occurred in any of the animals.

Six rabbits were each injected intraperitoneally, and ten each intradermally, with 1.0 c.c. of poliomyelitis virus during a period of five weeks. One animal was given twenty such combined injections during ten weeks. No symptoms developed. In a second group, nine rabbits were given ten intraperitoneal injections of 2 c.c. each and ten intradermal injections of 0.2 c.c. each of the poliomyelitis-vaccine mixtures. One was given twenty such injections. No symptoms occurred. Three other rabbits were injected intracerebrally with a mixture of 20 per cent poliomyelitis virus and 20 per cent suspension of normal rabbit testicle. One of this group showed a spastic condition of the hind leg. The other two died within thirty days, without having shown any symptoms of the disease.

At different times, a 20 per cent suspension of poliomyelitis-infected monkey cord was injected into the testicles of three adult rabbits. The testicles were removed in twenty-four hours and ground; a dose of from 0.2 to 0.3 c.c. was injected intracerebrally into three groups of young rabbits. A total of fourteen animals were injected, one of which showed definite flaccid paralysis of the hind legs in twenty-eight days. An emulsion of this cord injected intracerebrally into a monkey produced no symptoms.

Three rabbits were given 8 c.c. of a 20 per cent suspension of poliomyelitis virus by stomach tube on two successive days. A sterile irritation of the meninges was produced in them by injecting 0.3 c.c. of broth into the fourth ventricle at the time the second dose of virus was given. No reactions occurred.

Thompson was unable to produce an antipoliomyelitis serum in rabbits. He also failed in his efforts to adapt poliomyelitis virus to the organism of the rabbit and to produce poliomyelitis in this animal by testicular and intracerebral injections after testicular passage. Suggestive symptoms produced in very young rabbits were duplicated in nonspecifically treated and in uninoculated control animals. The virus of poliomyelitis did not survive twenty-four hours in the rabbit testicle, whether alone or mixed with vaccine virus. Repeated intraperitoneal and intradermal injection of poliomyelitis virus, poliomyelitis and vaccinia virus mixtures, or concentrated virus given by stomach tube in conjunction with meningeal irritation failed to produce the disease in rabbits. Although attempts to infect monkeys by intrastomachic injections and irritation of the mucosa with bile were entirely negative, some evidence was obtained to show that, if such procedures were repeated, an appreciable degree of immunity could be produced.

Harmon, Shaughnessy, and Gordon[19] called attention to the fact that Rosenau and Havens showed that any attempt in retransferring the infection in monkeys in the presence of a highly variable incubation period (two to forty-one days) detracts considerably from the strength of the argument that the condition produced was actually poliomyelitis. Identical findings of cellular infiltration were observed more in rabbits inoculated with normal rabbit brain and normal monkey brain than in uninoculated young rabbits. Once again it may be noted that most

of the reinoculations were made with material obtained from rabbits that died. This was particularly true of the material obtained from these animals which died on the fourth day, save for one (rabbit No. 55) which died on the fourteenth day and another (rabbit No. 14) which died ten days after the inoculation. One rabbit which was sacrificed five weeks after the inoculation showed changes almost similar to the micropathology of experimental monkey poliomyelitis.

They[20] concluded that young dogs, young cats, guinea pigs, mice, young pigs, lambs, and calves do not develop any condition recognizable as, or related to, poliomyelitis following massive inoculation of virus of established pathogenicity for monkeys. Although a small proportion of inoculated animals succumbed, death was due mainly to acute intercurrent respiratory diseases. One lamb had general weakness and another a noticeable limp in the right rear leg followed by prostration and death on the twenty-fifth day after inoculation. The autopsy findings in the latter were negative. Three other lambs about 3 months of age and weighing 20 kg. each, and three calves, two of which weighed 25 kg., and one, 30 kg., were obtained. Later two of the lambs and two of the calves were each injected intracerebrally with 5 c.c. and intraperitoneally with 100 c.c. of virus. The calves developed general motor weakness the day after inoculation, but not flaccid paralysis. They were found dead on the morning of the thirteenth day. The histologic examination was negative. No attempt was made to transfer the material from the calves or lambs.

Toomey[21] reported the production of paresis of muscles about the fetlock joints and hoofs of the hind legs of a horse after injections of "fortified" virus. Steppage gait developed, and the animal later had difficulty in walking. Its condition gradually became worse and finally involved the muscles of the hind legs, as well as those of the hoofs. The animal had difficulty in rising. When he was stood up, the legs spread apart.

Recently, Armstrong[22] reported that he was able to produce poliomyelitis in the Eastern cotton rat (*Sigmodon hispidus hispidus*) with the Lansing strain of poliomyelitis virus. Other strains were not infective. The same worker[23] reported that mice could also be infected by this strain.

COMMENT

There are many practical points to be considered from the standpoint of the practitioner. Can the lower animals harbor the virus of poliomyelitis? May they serve as carriers of the infection? Is the disease produced in them different from that appearing in man and the monkey? Why are smaller animals more resistant to the disease?

One may conclude that, in most experiments described in this paper save Armstrong's, the results were practically negative. If transmissibility did occur, it was infrequent, and the results were impracticable from an experimental standpoint.

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Round Table Discussion on the Business Side of Pediatric Practice

Hugh K. Berkley, M.D., Los Angeles, Calif.
Stanley Nichols, M.D., Asbury Park, N. J.
Secretary: John F. Carey, M.D., Joliet, Ill.

Round Table: "The Business Side of Pediatric Practice"
Dr. Hugh Berkley

CHAIRMAN HUGH K. BERKLEY.—At the June meeting of the Executive Board of the Academy it was suggested that a round table on "The Business Side of Pediatric Practice" might be sufficiently popular to warrant a place on the program. The idea met with favor.

Heretofore, round tables always have been scientific in nature. The chairman and assistants for each round table have been selected for their outstanding knowledge and ability in respect to the subject assigned to them. In that sense this round table is unique—neither Dr. Nichols nor I possess the slightest special ability in regard to our subject. It is also unique in that it is the first departure on the part of the Academy into a field which is not strictly academic medicine. The future of such lines of endeavor doubtless will rest on the popularity of this first adventure. That the subject would turn out to be an "adventure" was totally unexpected.

Thirty-five to forty years ago the men limiting themselves to the practice of pediatrics could have been counted on the fingers of one's two hands: Abraham Jacobi, Thomas Rotch, L. Emmett Holt, John Lovett Morse, John Howland, Samuel Clagett Busey, John Foote, J. P. Sedgewick.

Today this Society alone boasts a membership of 1,262 pediatricians, and the American Board of Pediatrics has certified 932 individuals as qualified to practice pediatrics as a specialty.

In the early days of the specialty of pediatrics those men who chose to limit their work to this field had a long hard struggle to gain recognition for themselves and their specialty from both the laity and the medical profession. Their success made it possible for those of us who have now been in practice some twenty to twenty-five years quite easily and rapidly to attain a fair modicum of success, both professionally and financially. This rapid success did not pass without notice and during the past fifteen years a steadily increasing number of men have entered the pediatric field. To a certain point this increase in number made it easier for all because it assisted in making the public pediatric conscious—to demand specialized service for the care of its children. Whether that point has been passed or not one cannot say with certainty, but it would seem probable that it has.

Other factors, unfortunately, have entered the picture, factors over which we have no control. Up to 1929 the pediatric profession seemed to be faring quite well. Private practice was well and profitably handled. The medical care of charity cases, to a large extent, was, willingly and without grumbling, absorbed by the profession at no cost to local or federal government. It may be freely admitted that charity work was not equitably distributed either from the standpoint of the profession or from that of the laity. This applied to all medical practice, not pediatrics alone. In spite of all that has been written and said in the past few years, the situation has been clarified but little.

Beginning with the year 1929 incomes began to drop, many to the vanishing point. Medical services remained an essential commodity, but the money needed to acquire them became difficult or impossible to obtain. Physicians' incomes decreased correspondingly. The amount of work to be done remained the same, perhaps increased, but there was too little money to pay usual fees for this service.

At this point local and federal governments began to enter the picture. We are all thoroughly familiar with the wilderness into which this has led, and we still stand without a Moses to lead the way out.

The entrance of government into the practice of medicine concerns the whole of our profession and in that way concerns us, but as pediatricians we have our own and separate problems which concern us individually and collectively and do not involve the profession in general. It is to these problems that this round table wishes to direct attention—the business side of pediatrics.

With the advent of the depression, with the resultant falling incomes and decreased collections, many men were forced by dire necessity to furnish more and more service for fees which they had adopted as their standard. A new form of competition appeared based upon quantity service rather than upon quality service as the standard of value.

This practice led obstetricians, who previously considered the child a pediatric problem from the time the cord was severed or certainly after his customary six-week post-partum care of the mother, to assume the responsibility of the infant's care during the period he considered the mother his patient. In some instances this meant only six weeks, but in many instances this was extended through the entire nursing period and often through the entire first year. Inasmuch as this extra service was rendered with no added cost to the obstetric fee, it is small wonder that that portion of pediatric practice which has to do with the feeding of infants rapidly dwindled, and the presence of a pediatrician in the nursery of a maternity ward has become a rare sight. This condition still exists today, and the certifying Board of Obstetrics now require a modicum of knowledge of infant feeding.

To offset this tendency, there has been a trend on the part of pediatricians to render services to well infants during their first year at a low flat rate on a written or verbal contract. These infant feeding services have become fairly popular with the public and in one form or another have been or are being used by a great many men. The variations used by individual men, in the same or widely separated localities, are too great to permit detailed discussion but will be taken up in a general way later in our discussion.

Somewhat along the same line, either because of the satisfaction gained by the doctor or by demand of the public, many men have devised flat rate services for the second and even the third year. Although not so frequently used as the first year service, those men who have adopted such plans speak highly of them. The various forms which have been used will also be presented.

Public health officials, school, city, county, state, and federal, always looking to the public good and to the strengthening of their own positions, have taken over a great proportion of what might be called the "preventive medicine"

portion of pediatrics. By this we mean the various immunization procedures. In the speaker's state, vaccination for smallpox, diphtheria immunizations, and rabies treatment all are furnished by school, city, or county health departments at no cost to the individual except as he may contribute to the general tax fund. To compete with this free service the pediatrician must furnish this service at a very nominal fee and render the service in such a high-class manner that the public is willing and glad to pay a fair fee for his superior type of service. This year the Los Angeles City School Department made available to every school child a free tuberculin test, and children having positive reactions were given chest x-rays at cost.

All of these free services, and many more which are being or will be added by public welfare departments, offer new obstacles for the pediatrician. Free infant welfare stations, serving all comers regardless of financial status, are now in operation in most cities. Many of these are manned by men untrained in pediatrics, but many are under the guidance of young, well-trained men who use the small salary to bolster the income from their meager private practice to a living wage. No one begrudges them this privilege, but it is a part of the business of the practice of pediatrics to compete with these free services and to lend every effort to see that free services are rendered to those needing free service and that it be denied those able to pay.

It was previously mentioned that pediatrics, as a specialty, had attracted a rapidly increasing number of men. We cannot say what the saturation point may be, but we are now forced to admit that competition has passed beyond the point of aggressive hard work and has entered the stage of competition on a fee basis. Many pediatricians, having expended much money and time properly to qualify themselves, are practicing pediatrics for the same fees that general practitioners demand and get. In no way is this intended to be derogatory to the general practitioners, many of whom practice pediatrics of high order by virtue of their native ability and their experience, but who have no capital investment in pediatrics as a specialty, either in time or in money. These men are gradually undermining their own specialty for it is certain that, either they must eventually raise their fees or, as is more probable, the rest of the men will be forced to lower their fees to meet them. No one can be denied the right to earn a living, and, if an individual must lower fees to the standard of the general practitioner, it certainly must be admitted as his privilege. However, if this becomes increasingly a necessity, it becomes a part of the business of the practice of pediatrics to lend a hand to the correction of the fault wherever it may lie; perhaps in educating fewer pediatricians.

Follow-up systems have both a scientific and economic value in pediatric practice. They will be discussed in some detail. Consultation work is of little scientific interest because one rarely learns either the outcome of the case or whether his advice was good or bad, right or wrong. It is of even less economic interest—carrying perhaps the largest credit loss of any part of practice.

With this general background in mind, it became important to get detailed information from many men in varied localities regarding their methods of handling these economic problems. To achieve this best the ubiquitous form letter seemed the only answer. Many of you are quite familiar with this letter. It was our aim to give those who chose to answer, the opportunity of expressing their feelings regarding various forms of feeding services for well infants, contracts for infant care, flat rate fees for immunizations, etc. We also requested ideas on other methods which had been tried in practice and found to have economic value.

It may not be amiss at this time to stress one point of importance. This round table was originated with the express idea of discussing the economic problems of pediatrics. That such problems exist, only the ostriches among us can deny. It should go without saying that in considering any economic factor it is understood that the quality of service rendered must not be lowered. Service must be kept at its present high plane and elevated when possible.

The generous response to our letter was our first adventure. One hundred fourteen men answered. Their answers indicated they had given the subject a considerable amount of time and thought. Many went to considerable effort to outline the background for their particular methods of procedure. Another adventure was that sixty men voluntarily expressed their pleasure both in complying with the request and in that the Academy had offered this opportunity for an exchange of economic ideas. The other men, with two notable exceptions, answered without special comment.

As to the exceptions, one person went so far as to voice his disapproval of the idea with the statement that "this subject has no place on your program . . . there are no ethical ways to increase the income of pediatrists except by honest professional work . . . if the Academy puts on this program, it will surely lose its position as an altruistic organization and cooperation with child welfare agencies will be compromised." The other stated: "I cannot see myself, in good times or bad, 'going into business' either for the purpose of increasing my financial returns or even for the purpose of making a living, if I were faced with that necessity" . . . "Even the title of the round table is not altogether pleasing to me."

Medicine is an altruistic profession, and to some degree all medical men are altruists. I think all of us would be pure altruists if we were situated financially so that monetary matters gave us no concern. The facts are quite to the contrary. Most of us must make a living. Personally, I cannot bring myself to feel that the fact that I must make a living out of my profession in any way degrades either me or the profession. On the contrary, I believe that by virtue of my dependence on my profession, it stimulates me to do more and better work in order that I may maintain my professional standing and its associated income.

Owing to the fact that a large number of quite long letters were received, it was impossible to write a complete answer to each author. A post card of thanks was sent to each one, and the chairmen wish at this time to thank every man who took the time and the pains to answer the questionnaire. These answers have been carefully studied and tabulated, and they form the background for the direction of this round table. In doing this analysis, we could not but feel sympathy for Esther Everett Lape who compiled the data in the two-volume report, "American Medicine, Expert Testimony Out of Court."

Some letters contained outstanding statements which seemed of sufficient value to classify separately. This I have done under the heading of "Impressive Statements." Some of these statements contradict others, and where such is the case you may be sure that each statement was made by a man with an "impressive" name in pediatrics. These will be read at the end of this portion of the discussion.

The fact that 60 out of 114 answers expressed gratification that economics had been given a place on the program leads the chairmen to believe that the Executive Board were justified in their decision. The attendance at the round table seems to approve of their action.

From the answers received it is evident that infant feeding services rendered on contract or on a fixed fee plan occupy first place in point of interest. Tabulation shows that 54 of the 114 men answering the questionnaire use some form of this service. The types offered are as follows:

1. *Signed Contracts.*
   a. Full service, unlimited office visits, house calls, telephone service, immunizations, etc. Rates $60 to $250 per annum.
   b. Well baby service. Full office service, sick or well, telephone service, immunizations. $35 to $100.
   c. Well baby service. Limited office but including telephone and immunizations. $35 to $75.

2. *Verbal Agreements.*
   a. Full service as in 1 a. $60 to $85.
   b. Well baby service. Full office service as in 1 b. $50 to $82.
   c. Well baby service on monthly basis; limited or unlimited visits; with and without immunizations; full or limited telephone service. $3 to $10 per month.

By far the more popular type of service is the latter group. The limitations are widely varied. The majority of men exclude house calls; most men include the immunizations, and the fee most often charged is $5 per month. The allowable office visits vary from one per month to an unlimited number. It is worthy of comment that none of the men complain that they are abused by the patient's demanding too much service.

Thirty-eight men have never tried any form of "agreement" type of service. Only one man stated he had tried this type of service, found it unsatisfactory, and discontinued its use.

That we may have more time for discussion from the floor, I have listed many of the points brought out by the answers to the questionnaire; suggestions which have been put forth as worthy of comment; methods which have been found successful in maintaining a high type of service to the patient and satisfactory income to the doctor.

1. *A Telephone Hour.*—Four men have set aside one hour a day for parents to call in for discussion of their problems. All attest to its value.

2. *A Telephone Follow-up.*—Several men make it a routine practice to telephone the parents of ill children after house calls have ceased to be necessary. The production of good will far exceeds the time, effort, and expense involved.

3. *Return Appointments With Follow-up.*—Many men, for their own as well as the patient's benefit, make return appointments at the time of each visit. If the appointments are not kept, a reminder (telephone or card) is sent to the parent. This allows the physician to keep in active touch with his patient and assures the parents of the doctor's interest in *their child.*

4. *Immunization Notices.*—Many men have found it of value to put a footnote on all diet lists stressing the importance of immunization procedures.

5. *Health Cards.*—Some men issue health cards stating when and what immunizations have been completed. These cards stimulate parent interest in seeing to it that prophylactic measures are carried out.

6. *Follow-up on Schick Tests and Vaccinations.*—It is sound medical practice to repeat Schick tests in five years and vaccinations in from five to seven years. A reminder file and a post card to parents result in the return of a fair percentage of these children for retesting or revaccination.

7. *Immunizations.*—School and health departments often do these prophylactic procedures at the cost of materials or free. Low fees for these services with a substantial reduction if all immunizations are given are recommended by several men. Many men include the immunizations in their charge for the first year of infant care. Given separately the most commonly used fees are (a) diphtheria, 2 or 3 doses and Schick test, $10; (b) pertussis, 3 or 4 doses, $8 to $10; (c) vaccination, $2 to $3, $5 when re-dressed several times.

8. *Flat Rates for Child Care in Second and Third Years.*—This is not a widely accepted procedure but apparently is quite satisfactorily used by a number of men. Fees vary from $9 to $60, depending on amount of service allowed.

9. *Discounting Bills.*—Several men offer a discount of 10 per cent on bills paid before the 10th, 15th or 20th of the month.

10. *Miscellaneous Points.*

a. Don't offend older children by having your waiting room too much like a kindergarten.
b. The Academy should discourage low and cut-throat fees.
c. Academy members in a given district should get together on fee schedules.
d. In Ontario, Canada, a section on pediatric economics has been formed as an adjunct to the scientific section.

Impressive Statements

1. "Do your own tonsils and adenoids and minor surgery, if you can do them well."
2. "It seems to me this subject has no place on the program."
3. "Little things, if done in a systematic manner, take very little time and thought, and they have paid dividends both in increasing collections as well as increased service to the individual patient."
4. "Medical men, in general, and pediatricians in particular, are doing more and more for less and less, and if this situation is not corrected, we will soon be doing everything for nothing."
5. "Doctors are such poor business men that they have never stopped to figure the actual cost per patient."
6. "I am strongly convinced that the backbone of the pediatrist's practice, both from the standpoint of the good he can do and his own financial welfare, is preventive medicine, which involves regular examinations."
7. "Credit managers of sound business firms can teach us a great deal. Since we began 'taking lessons,' our credit losses have dropped to less than 1 per cent."
8. "Physicians' services, even of the high standard which we know today, probably can be better distributed and the fair costs thereof can be more economically provided without necessarily lowering the quality we now enjoy at the hands of the best trained men in the profession."
9. "The best professional man can better serve his patients by being more business-like in the use of his available time, and this efficiency results in economy which can be shared with his patients."
10. "In the practice of medicine I do not think it is proper to organize in any way for the purpose of increasing financial returns. I do not believe there should be uniformity anywhere. The doctor is, above all, an individualist."
11. "I believe we, therefore, are practicing better medicine than we would be under the fee per visit system."
12. "I have perhaps received the greatest satisfaction from this method (yearly flat rate) of practicing because I can give the patient who needs it unlimited care."
13. "I am a darned good doctor but a darn poor business man."
14. "Without a question the round table on 'The Business Side of Pediatric Practice' will be the most popular discussion we shall have at the meeting."
15. "We should keep the financial side of our work on a par with our scientific standards."
16. "In some ways, pediatricians are directly responsible for a lowered volume of business. Two great errors, in my opinion, are tonsillectomies performed by pediatricians and the selling of 'feeding services.'"

17. "I know that the 'free list' should be cut down. Naturally, I believe that doctors should not charge doctors' immediate families for medical services, 'dog cannot eat dog,' but the extent to which this professional courtesy has been expanded is ridiculous."
18. "The marked change in the economic status of the country during the past ten years and the more recent tendency to increased socialization in the medical field have made it imperative for all physicians to revalue their services not only from their own viewpoint, but, more important, from that of the public."
19. "There will have to be a definite standardization of services, or competition will lower us to commercialism."
20. "Pediatrics is a very worth while and most interesting branch of medical practice, but, financially, is severely handicapped."
21. "Health program policy, which is carried out in the public schools, may conflict with the business side of practice when no influential physicians are informed about that program. When there is such a conflict, the school policy is unsound—educationally and socially."
22. "To enhance their position (the obstetricians) they have taken the control of the obstetrical nurseries away from the pediatrician, which means, of course, that they will go back to the old system of looking upon the newborn infant as a by-product. I feel that the American Academy of Pediatrics should bring pressure to bear . . . so that these babies may again be returned to the care of the pediatrician."
23. "I don't propose to outline what I believe should be in the program of health service contracted for from year to year, but I believe pediatricians should work out a definite plan not only applicable to the infant under one year but to be carried on year by year."
24. "I think the national societies of obstetricians should be approached on the subject of obstetricians' taking care of infants during the first year of life and longer."
25. "I am afraid flat rate fees for any year of the patient's life, for immunizations, or for feeding services for infants, may eventually turn out to be an entering wedge for state medicine, which we are all trying to ward off."
26. "There is nothing wrong with the specialty of pediatrics. The pediatrists are the finest group of men in medicine today."

All of these things and many others are a part of the business side of the practice of pediatrics. This is your round table. It is for you to ask questions freely and to discuss the points of interest. The leaders occupy their positions only to order the discussion so that valuable time and opinions may not be lost. To attain that end we request that all discussions be kept strictly to the subject at hand.

CHAIRMAN STANLEY NICHOLS.—Dr. Berkley has most ably taken up the mechanics of pediatric practice and reasonable fee schedules, etc. I should like to take up pediatric practice, both private and particularly public, from another angle, covering two points.

1. How can we develop the improved quality of private and public pediatric practice?

2. How can we educate private patients and public groups to recognize good quality pediatric service and pay reasonable fees for such service? (Virtually salesmanship producing a better service and reasonable methods of stimulating the use of such service.)

There are four types of private and public Pediatric Practice, as follows:

1. *Private Practice.* The pediatrician's individual care of children.
   (There is a public angle of private practice: (a) state license to practice; (b) legal requirement to practice with reasonable ability and care.)
2. *Voluntary Health Insurance* administration by
   a. Nonprofit group
   b. Medical society or
   c. Ontario, Canada, plan—combination agency.
3. *Group or Mass Practice* in
   a. Hospital clinics
   b. Hospital ward service
   c. Baby health conference
   d. Preschool or Child Health conference (P.T.A. summer round-ups, etc.)
   e. School health service
   f. Service in child guidance or other mental hygiene clinics for adolescents
   g. Other miscellaneous service, such as the pediatric side of crippled children's clinics, tuberculin testing clinics, immunization clinics, etc.
4. *Compulsory Health Insurance* under public administration, so far undeveloped in the United States.

This type necessitates immediate and careful study, both because of its imminence and the great probability that, in spite of civil service and merit systems, the insidious evils of political bossism and political patronage systems of personnel appointments and other factors, will almost certainly force this into being the poorest quality of public pediatric practice. The political threat of this type of practice is most menacing and threatens to develop the deplorable spectacle of *poor* medical service to the low-wage group. All of us who have had experience with political patronage and its attendant evils are well aware of this grave danger to good medical care of children, and we hope that this catastrophe to the quality of pediatric service may, after careful consideration by all concerned, be indefinitely postponed or avoided, until the time arrives when the American people, as a whole, suppress the present evident evils of the political patronage system and its obvious unfortunate effect on all public health and child health development.

1. How can we improve the quality of pediatric practice, both private and public?

We can improve the quality of pediatric practice by improving the training of pediatricians, and by increasing their participation in all forms of child health building programs, and by improving the distribution of their pediatric services.

We here present six methods of improving the pediatrician himself in his various capacities which include the following:

a. Private practice
b. Consulting practice
c. Teaching
d. Hospital pediatric training
e. Attendance of pediatrician at public and child health conferences
f. School physician
g. Attendance of pediatrician at various types of clinics, crippled children's clinics, tuberculosis clinics, immunization clinics, etc.

1. By improving pediatric *undergraduate education*
   a. Undergraduate education of medical students
   b. Education of nurses, etc.

Wherever possible pediatricians should take part in such teaching. Opportunities are limited for the teaching of medical students, but frequently available for the teaching of pediatrics to nurses. All such teaching improves the pediatrician himself.

2. By the continual improvement of the *pediatric education* of the pediatrician himself

a. By studying pediatric literature (up-to-date books, medical journals, reprints)

b. By taking, whenever possible, short courses covering outstanding pediatric problems. (The Academy round tables are outstanding opportunities in this field, and regional meetings and other pediatric medical meetings offer much in this regard.)

c. By improving his pediatric knowledge by serving in as many of the fields of clinical pediatrics as possible in addition to private practice

(1) Hospital service (newborn, ward, and out-patient pediatric service)
(2) Infant health stations
(3) Preschool health conferences (including P.T.A. summer round-ups)
(4) School health services
(5) Adolescent health service, child guidance clinics, mental hygiene service
(6) College health services
(7) Miscellaneous health work for organizations (P.T.A., American Legion, boys' clubs, women's clubs, crippled children's clinics, tuberculin testing clinics, immunization clinics, etc.)

3. By thorough *development* by our American Academy of Pediatrics of *complete child health programs* for building better health for the children of America. (The American Academy of Pediatrics is the child health builder of America.)

Such as

a. American Academy of Pediatrics standards for child health supervision and care

b. American Academy of Pediatrics child health records—now being developed (one, short for group work; two, comprehensive for private practice)

c. American Academy of Pediatrics score card for parents (regarding adequacy of child health care received by any given child)

d. American Academy of Pediatrics certificates to be given to faithful parents for good care of children in different age groups, to be attested by Academy Fellows, as certified specialists in the child health field.

Certified babies to age 2
Certified preschool children to age 5
Certified primary and grammar school children, to age 12
Certified high-school children, to age 18 (approximately)
Certified college students

4. By improving the pediatrician's *knowledge of mental hygiene* of children, and his services in this most important, neglected field. In order to do this, the pediatrician must have greater knowledge of the psychological and psychiatric problems of parents and children and what the pediatrician can do to help solve these problems.

Among these must be included:

a. The training of habit attitudes in the *parents* as regards babies and children

b. Proper habit training in the *child*

c. Study of good parent-child relationships and what family adjustments are needed

d. Proper sex education

e. Proper vocational guidance

f. Other mental hygiene problems which present themselves

(An outstanding contribution to mental hygiene as well as the development of good pediatric service, is that each pediatrician make clear to the parents that, with his special knowledge, he is most anxious to largely carry the *worries* of parents, and only asks for their faithful cooperation in order to help develop the best possible physical, mental, and if you will, spiritual health for each child.)

5. More *participation*, both *individually* as a pediatrician, and *collectively* as a member of professional societies and citizen groups (such as Academy of Pediatrics, county and state medical societies, civic organizations, etc.) in helping to improve the quality of medical pediatric service given in all forms of pediatric practice, particularly in

a. Hospitals, out-patients, in-patients

b. Child health conferences

c. Child health service for public agencies (health departments, welfare departments, crippled children's division, etc.)

d. Child health services for private agencies (P.T.A., American Legion, boys' clubs, service clubs, women's clubs, etc.)

e. School health services

f. All other child health services

6. The improvement of the *mechanics of private practice* and the *distribution of pediatric services*, which have been completely covered by Dr. Berkley's able presentation.

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2. How can we educate the private patients and public groups to recognize good quality pediatric service and pay reasonable fees for such service?

By educating the four main groups on two points: What constitutes good quality pediatric service and reasonable compensation for same; and the Academy child health building program. The four main groups to be educated are: private patients, professional health service groups, public (official) agencies, and private health and welfare agencies concerned with child health.

1. *Education of Private Patients.*

a. The pediatrician must first sell himself to the private patient as to (1) kindly personality; (2) thorough training; and (3) sincere interest in the health of the child.

The four questions a parent asks concerning a physician are:

1. Is he well qualified in his professional work?
2. Is his work thorough?
3. Does he demonstrate sincere interest in the child's health?
4. Does he charge reasonable fees?

b. Education of parents as to the American Academy of Pediatrics standards of child health supervision.

c. Education of parents to the use of the Parents' Score Card.

d. Education of parents to keep for each child a Home Child Health Record.

e. Education of parents to work for health certificates for each child in each of the afore-mentioned age levels.

f. Education of parents by providing, in the pediatrician's office, concise child health literature (one sheet, if possible) such as:

(1) The American Academy of Pediatrics Child Health Supervision folder
(2) Folder on breast feeding
(3) The American Academy of Pediatrics pamphlet on immunization
(4) The American Academy of Pediatrics Contact Infection folder, "For the Sake of the Child"
(5) "Prepare Your Child for School"
(6) Folders on habit training
(7) Pamphlets on good habits for adolescents, etc., etc.

2. *Education of Professional Health Service Groups.*

(In the education of public groups, professional, public official, and private health and welfare agencies, the pediatrician should, if possible, secure training in methods of discussion, conferences and public speaking, as these are indispensable to the carrying on of this type of education.)

The education of professional health service groups and the groups which follow can best be done by holding repeated conference discussions as to

a. What constitutes *good quality* of medical pediatric service.
b. Standards of child health supervision—child health building programs.
c. Reasonable compensation for good quality service.

This education should cover, as a minimum, the following professional service groups:

a. Medical societies (state, county, local, special)
b. Dental societies
c. Nurses' organizations—particularly public health nursing organizations
d. Hospital officials and workers
e. Pharmacists' organizations (a powerful and too-little used ally of the medical profession)
f. Medical social workers.

3. *Education of Public Official Agencies.*

The education of public official agencies can best be done by holding repeated conference discussions as to what constitutes

a. Good quality of medical pediatric service
b. Standards of child health supervision and child health building programs
c. Reasonable compensation for good quality service.

This education should cover, as a minimum, the following groups of public officials responsible for child health:

(a) Health officials, (b) welfare officials, (c) school officials, (d) crippled children's officials, (e) civil service officials, (f) Department of Labor officials, (g) other public agencies having to do with the health of children, such as state boards of children's guardians, etc.

4. *Education of Private Health and Welfare Agencies Concerned With Child Health.*

The education of private health and welfare agencies concerned with child health can best be done by holding repeated conference discussions as to what constitutes

(1) Good quality of medical pediatric service
(2) Standards of child health supervision and child health building programs
(3) Reasonable compensation for good quality service.

This education should cover, as a minimum, the following groups:

a. Tuberculosis associations
b. Social hygiene associations
c. Private child caring agencies
d. Private schools
e. Labor organizations
f. Farm organizations
g. Parent-Teacher Associations
h. American Legion child welfare committees

i. Fraternal orders interested in crippled children and child welfare
j. Service clubs interested in child health
k. Women's organizations interested in child health
l. Maternal center organizations
m. Birth control leagues
n. Sterilization leagues
o. Visiting Nurse Association
p. Mental Hygiene Association
q. Child welfare organizations
r. Hospital service associations
s. Voluntary health associations
t. Medical cooperative associations
u. Other health cooperative associations
v. All other private health and welfare agencies interested in child health

Dr. Berkley and I wish therefore to provoke discussion as to improving pediatric practice, on three points.

1. Distribution of pediatric services, fee schedules, and the mechanics of rendering good pediatric service to our private patients.

2. The constant improvement of the quality of our pediatric service.

3. The very important problem—the education of our private patients and the four public groups in the matter of high quality public and private pediatric service and reasonable compensation therefor.

DISCUSSION

The early part of the discussion was taken up with "contract practice." The term in itself was distasteful to most of those present, who preferred some other terminology such as "infant health service." A few had regular written contracts and the question arose as to whether or not they were legal and binding. Also the question of a case under contract if the patient required treatment during the physician's absence from the city.

DR. R. A. HIGGINS (PORT CHESTER, N. Y.).—The service is a gentleman's agreement. My experiences with agreement practice have been highly satisfactory to me and to my patients. I make no definite appointments but have a follow-up system whereby the patients are called and voluntary appointments made. I consider it a valuable public health measure.

DR. S. P. WAINWRIGHT (BIRMINGHAM, ALA.).—Many of the patients in my territory are in the $2,000 income class and often some below; they are able to afford and are delighted with the service. I found it very satisfactory.

DR. W. C. FARGO (CLEVELAND).—My contract specifies the number of calls at the office and home, examination at the hospital, and immunization. I have never felt the contract was abused.

DR. T. A. GIBSON (WINCHESTER, VA.).—Were the questionnaires sent to men in smaller communities?

CHAIRMAN NICHOLS.—A representative list was chosen in the requests for answers to the questionnaire in that every type of community was chosen both as regards location and population and number of pediatricians.

DR. K. G. WOODWARD (ROCKFORD, ILL.).—I have never had a contract practice and have only rare applications for it. I should like to hear from men in smaller communities and also about the possibility of increasing it to include older groups, such as the school child and the adolescent.

DR. A. D. BIGGS (CHICAGO).—I had a contract practice for an industrial plant in a small city before entering upon pediatric practice. It was very unsatisfactory and was very much abused; it produced an excessive amount of office work.

CHAIRMAN NICHOLS.—It is a surprising fact that more men did not complain of this in answering the questionnaire.

DR. R. A. CRAIG (KOKOMO, IND.).—I do not approve of contract practice because it might become general. More individual attention is given to noncontract patients.

DR. G. M. CLINE (BLOOMINGTON, ILL.).—I have never had a contract practice. A great deal of my work is consulting. I always write the physician who has taken care of the child giving my opinion of the case and treatment necessary. I have now included allergy in my work and believe the pediatrician must be able to render all the special services, as he is competing with the general practitioner who is new from refresher courses and modern medical school education and is much more adept in child care than he was twenty or even ten years ago.

The discussion had become so confusing that it was suggested that a vote be taken of the men doing contract work and those not doing it. A surprising fact was that less than 15 per cent of the men were rendering this type of service. Fifty-eight voted.

The question as to the type of a waiting room was brought up, especially as regards older children. The adolescent child naturally does not care to wait in a room fixed up for the kindergarten age.

CHAIRMAN BERKLEY (LOS ANGELES).—The pediatrician is a general practitioner caring for all the ills of the age group from infancy through adolescence. This naturally may include at the physician's discretion, the referring of minor cuts and fractures to another specialist.

DR. J. F. CAREY (JOLIET, ILL.).—I am of the opinion that a correlation of value of medical specialties within the profession must be considered in order that proper care may be rendered without too much of an extra burden on the family exchequer.

DR. G. WEINFELD (HIGHLAND PARK, ILL.) asked for an opinion concerning night calls and DR. S. D. MILLS (WESTFIELD, N. J.) asked concerning telephone calls.

CHAIRMAN BERKLEY.—People usually expect to pay more for night calls, and the matter of telephone calls must be judged by the type of service given and the frequency.

DR. R. VON ACHEN (PEORIA, ILL.).—I think the time element involved in caring for a patient or the severity of the case should have some bearing on the charge for the service. I feel that the present setup of agreement practice is too commercial.

DR. H. E. VAN RIPER (MADISON, WIS.).—What should be the fair percentage of net income of gross income?

CHAIRMAN NICHOLS.—The A. M. A. has figures. Some spend 20 per cent, others 60 per cent of the gross. The average amount of the gross is 40 per cent.

DR. P. J. WHITE (ST. LOUIS).—Collective measures are coming. I have been opposed to the annual service plan partly because of the extra hours which would be devoted to the telephone. If we are very conscientious, it may not be well to standardize. Average infant cost is $49 per year for office.

CHAIRMAN BERKLEY.—Do you have case histories that average $49 per year?

DR. WHITE.—I do not know whether fees run that high.

CHAIRMAN BERKLEY.—I have practiced both methods. The yearly plan in my own office offers tremendous advantages. Furthermore, at the end of the year the patient is likely to be with you.

DR. WHITE.—What do you do about the telephone?

DR. D. C. MEBANE (TOLEDO, OHIO).—My charges average $75 per year without flat fee service.

DR. A. C. GIPSON (GADSDEN, ALA.).—I had a good deal of pioneering to do in an industrial town. All the plants were under contract plan. I soon started a service plan for the well baby. Illnesses outside were extra. I soon found that my income was greater per patient, and the plan is becoming fashionable in this city. People are coming more often, and others who would not ordinarily be seen at all during the first year. The annual rate for health is $25 cash, or $30 in monthly payments. Telephone calls are rarely excessive after the first few days the new baby is home. The average total cost is $40 to $50. I include diphtheria immunization. Pertussis injections are extra. Towns (several together) total 50,000.

DR. E. B. BRANDES (CINCINNATI).—What does economic status have to do with fee?

DR. GORDON MANACE (TORONTO, ONT.).—The contract system was foisted on me four or five years ago. Fees in Canada are less than in the United States—average office fee is $2 or $3. Many people in the working class group are willing to pay $35 per year. These people otherwise ask $2 fee on noncontract. Golf club people also wanted contract which was overcome by charging $45 to $50 for the better economic class. I care for well babies only but see them as often as the parents desire. It has cut down tedious conversation by phone. The satisfied parent is the best advertisement. Some come as high as 22 times.

DR. R. D. SCHIRACK (CANTON, OHIO).—Do you use an appointment system on the yearly plan? [Yes, by vote.] How do you determine operative fees so that they are fair to child and his family? I think the pediatrician knows what the family can afford.

CHAIRMAN NICHOLS.—I think the matter of operative fees can best be discussed and settled in your own medical societies.

DR. HARRIS HOSEN (PORT ARTHUR, TEXAS).—I practice in a refinery town and charged $60 per year. I found it hard to differentiate between the well baby and illnesses in basing fees; consequently, I included whole bill. I stopped last year, indirectly told by the medical society.

DR. FAIRFAX HALL (NEW ROCHELLE, N. Y.).—I object to the word "contract"; better call it "infant health service." I feel you can ask parents to bring infants in freely, and at the end of a year I think one has better babies. I believe in making the plan flexible.

1. All—blood, urine, etc., examinations, house visits 50 per cent discount on flat rate.
2. Intermediate without house visit.
3. Office only.
4. Special arrangement. Some people want house visits only.

CHAIRMAN NICHOLS.—How much overuse of house visits?

DR. HALL.—I have found it less since using a half fee for house visits.

DR. J. J. YORK (SCHENECTADY, N. Y.).—I think the type of practice depends upon the opposition of the medical profession in your city. One pediatrician was threatened with removal from the society. It also depends upon income of man; if he is young, he may need extra practice; if older, with annuities, he may not be interested. Personally, I think we will all be driven to some fee basis for services rendered. I perform all my tonsil and adenoid operations and keep the patients in bed; the ear, nose and throat men let the children up and about too soon. I do the tonsillectomies and adenoidectomies, but never in the winter. I charge $15 for

the diagnosis of appendicitis, but do no more unless the patient wants me to call. My surgeons are guided by what the pediatrician advises. Hospital calls are additional, if parents desire them.

DR. W. E. VAN ORDER (CHATTANOOGA, TENN.).—The plan was tried in this town of 150,000 and seemed popular. But the first man charged $60, later dropped to $50—efforts of one man to get more business by undercutting. How do you collect? Cash, monthly, or termination of plan? I believe care on yearly basis is favorable for the first year. T.V.A. employees are accustomed to yearly service.

CHAIRMAN BERKLEY.—The collection on plans varies widely. Some physicians demand six months' cash down, some, payment quarterly; and some, payment monthly.

DR. R. W. HOLT (NIAGARA FALLS, N. Y.).—We have no interns, so the referring physicians assist surgeons, and charge $25 for assistance and are responsible for postoperative care. I render separate bill. For first four months, I charge $5 per month and see the patient twice in the office.

DR. J. W. BRUCE (LOUISVILLE, KY.).—What is the right thing to do about newborn infants? I find it difficult to collect more than $12 to $15 if I see the infant every day.

DR. MEBANE.—I charge $5 for visits to newborn infants in the hospital so as to get confidence of parents and get new babies to take care of.

DR. WHITE.—I visit the newborn infant shortly after birth and before discharge from hospital and charge for two visits. Regarding the question of pediatricians opening eardrums—I think this depends on the community and qualifications. In St. Louis, one should offer opportunity to call in otologist.

DR. E. T. McENERY (CHICAGO).—In regard to the yearly health service, do the pediatricians offering this plan give twenty to twenty-five minutes per patient? Do they sit down and discuss the individual problems? In some cities, offices are operating all day. In Chicago, distances are too great to include house calls. I drive 1,200 to 1,500 miles per month and may include many hospitals. How do you make house calls in Los Angeles? How do you handle the telephone?

CHAIRMAN BERKLEY.—You are approximately correct about distances in Los Angeles, e.g., three calls, fifty miles. Our service is for the office only; one office visit per month. Our office telephone is covered by twenty-four-hour secretarial service, which has cut down home telephone calls 20 per cent.

CHAIRMAN NICHOLS.—Telephone problem. One free hour. Charge $1 to $2 outside of that hour, unless emergency. Charge for phone before depression $8; after, $3.

In trying to make older child comfortable in office, do you put circus out of way?

DR. YORK.—No circus, etc., on floor.

CHAIRMAN NICHOLS.—How do you hold adolescents?

DR. HOSEN.—I think one should get interested in work in chronic diseases, such as chronic respiratory diseases and allergy. One should also have an interest in childhood psychology.

DR. VAN RIPER.—The allergists rule out all. I think allergy is a field to increase the volume of business by common sense and effort.

CHAIRMAN BERKLEY.—How many do your own work in allergy? (Fifty per cent, by count.)

CHAIRMAN NICHOLS.—The Michigan State Medical Society has a plan for medical care which is for a period of illness in a hospital rather than any specific illness. (Poll on health service plans, 25 per cent.)

DR. HOSEN.—The retail merchants organized a loan agency. No one can borrow without paying all creditors.

DR. C. L. RUGGLES (CLEVELAND.).—I think part of the problem can be managed by diversification, e.g., mental hygiene. How can revenue be measured with time spent? A mother can outpour problems for months past. Conferences can last as long as two hours or more. I have tried to set a rate per hour.

CHAIRMAN NICHOLS.—From the conversation this morning, I think that most of us are giving honest effort and are seriously concerned by rates the patient can pay. I think that rates should be commensurate with ability to pay. How much time do you average per patient in the office?

New	30 minutes.	All but two.
New	20 minutes.	Two
Old	30 minutes.	Five.
Old	20 minutes.	Twenty-five.
Old	15 minutes.	Six.

DR. J. K. EVERHART (PITTSBURGH).—I have been in offices where forty-five to fifty-five patients were seen in an afternoon.

Dr. F. P. GENGENBACH (DENVER).—I could have commented on every issue. I have grown up from individual practice to one with three partners. We have a clinic building uptown which has solved the parking problem.

Five years ago I sent out a query, money not considered. Five years before and after the depression.

Amount of surgery? Tonsils, myringotomy?

Periodic health plan. (Dr. Gengenbach gave card on plan to Dr. Berkley and Dr. Nichols.)

At first we had a variety of plans, now we are on a fixed plan. I'm sort of an idealist. I would like to do all that I felt should be done and do without charging patient too much. Later we put in allergy department, do blood count, x-ray, etc.

DR. MARTHA ELIOT (WASHINGTON, D. C.).—I am wondering what is the income of the families that come under this type of service? I suspect there is a great range. What is the bottom level on this type of service?

CHAIRMAN NICHOLS.—Thirty-five dollars for the office; $20 to $30 plus for house. Incomes vary. Do majority come in $1,200 to $2,000? Majority give (half) discount under $1,200 year level?

DR. GENGENBACH.—In families with incomes of $1,500 and under, infant mortality is higher. Probably the parents are not in financial condition to obtain good medical care.

CHAIRMAN NICHOLS.—Where do you begin to make discount?

$2,000 and up	0
$1,500	10%
$1,200	10%
$1,200 below	Free

In closing, I wish to stress the fact that the Academy is making every effort to adjust fees to such an extent that pediatric services may be available to all wage groups.

PERIODIC PHYSICAL EXAMINATIONS OF THE HOSPITAL PERSONNEL AMONG CHILDREN'S HOSPITALS OF THE UNITED STATES AND CANADA

THE Committee on Hospitals and Dispensaries conducted a survey to determine what methods and procedures are practiced in the children's hospitals of this country and Canada to protect the patients from infections which may be acquired from individuals of the hospital personnel. This contact may be direct or through the handling of food.

Questionnaires were sent to 33 children's hospitals. Twenty-six questionnaires were returned with the required data. From one hospital it was reported that so far adequate physical examination is given only to nurses. The questionnaire was not returned from six hospitals. The data received from the 26 hospitals is tabulated, with the necessary explanatory remarks, in the same form as the questionnaire used.

Are members of the attending medical staff examined or checked for evidence of the following diseases?

	YES	NO	IF YES, HOW OFTEN?
1. Pulmonary tuberculosis	1	25	once
2. Syphilis	1	25	once
3. Gonorrhea infection		26	
4. Typhoid carrier		26	
5. Dysentery { infection / carrier		26	
6. Other contact infections of similar nature		26	

The one hospital which reported examinations for tuberculosis and syphilis at the time of employment is a part of a medical school where the attending staff is on a full-time basis.

Are members of the intern and resident staff of physicians examined or checked for evidence of the following diseases?

	YES	NO	IF YES, HOW OFTEN?			
			EVERY 3 MONTHS	WHEN INDICATED	YEARLY	ONCE
1. Pulmonary tuberculosis	13	13	1	2	3	6
2. Syphilis	3	23		1		1
3. Gonorrhea infection	2	24		1		
4. Typhoid carrier	3	23		1		1
5. Dysentery { infection / carrier	2	24		1		1
6. Other contact infections	3	22		2		1

No hospital requires a complete examination of its intern and resident staff. In 13 hospitals no examination is required while in 7 others only examinations for tuberculosis are performed. The few other examinations are performed usually only when indicated.

Are members of the nursing staff examined or checked for evidence of the following diseases?

	YES	NO	IF YES, HOW OFTEN? EVERY 3-6 MONTHS	WHEN INDICATED	YEARLY	ONCE
1. Pulmonary tuberculosis	21	5	3	1	9	6
2. Syphilis	12	14			2	9
3. Gonorrhea infection	6	20			1	4
4. Typhoid carrier	10	16		1	2	3
5. Dysentery { infection	6	20		1	3	2
5. Dysentery { carrier						
6. Other contact infections	13	12		3	1	2

Complete examination of nurses is required in 5 hospitals (except for syphilis in one), while in 5 no examination is made and in 5 examination is only for tuberculosis. In a few reports it was stated that only the student nurses were examined and not the graduate nurses.

Are maids, orderlies, and other workers coming in direct contact with patients examined or checked for evidence of the following diseases?

	YES	NO	IF YES, HOW OFTEN? EVERY 3 MONTHS	WHEN INDICATED	YEARLY	ONCE
1. Pulmonary tuberculosis	18	8	1	1	2	8
2. Syphilis	14	12		1		9
3. Gonorrhea infection	8	18				5
4. Typhoid carrier	7	18		1		2
5. Dysentery { infection	5	20		1		2
5. Dysentery { carrier						
6. Other contact infections	7	18		1		2

Complete examinations of maids, orderlies, and other workers are required by 5 hospitals (except for syphilis in one), not required in 8, and examinations for tuberculosis only are made in 3 others.

Are kitchen workers—cooks, food handlers, etc.—examined or checked for evidence of the following diseases?

	YES	NO	IF YES, HOW OFTEN? EVERY 3 MONTHS	WHEN INDICATED	YEARLY	ONCE
1. Pulmonary tuberculosis	18	8	1	1	5	7
2. Syphilis	18	8		1	5	8
3. Gonorrhea infection	12	14			3	4
4. Typhoid carrier	12	14	1		3	5
5. Dysentery { infection	12	14	(6 mo.) 2		4	3
5. Dysentery { carrier			(6 mo.)			
6. Other contact infections	10	15				5

Eleven hospitals require complete examinations (except for syphilis and gonorrhea in one each) of its kitchen workers and food handlers. In five hospitals no examination is required, while in one other only for tuberculosis.

Does your staff believe that it is advisable to have such examinations made at { time of employment / or / regular intervals?

Yes—Both 16
No—Both 3

If not, what reasons for not believing this advisable?

Three stated examination at time of employment was sufficient.

One stated examination should be made at regular intervals.

One stated theoretically examinations should be made, but they have had no difficulty even though they were not done.

Two stated the hospital had as yet no policy as to examinations.

One stated that examinations of nurses was necessary, but not of interns and staff.

Have there been incidents in the history of your hospital in which evidence strongly suggested that such diseases as tuberculosis, syphilis, typhoid infection, dysentery infections, or other contact infections have been transmitted to patients through contact with some individual of the attending or hospital personnel?

Fifteen reported no transmission of infections to their knowledge.

One reported spread of diphtheria through a maid and probable cases of scarlet fever from nurses.

Four reported spread of respiratory infection.

One reported questionable transmission of mumps once.

One reported one suspicious incident of transmission.

Two reported transmission of syphilis and tuberculosis from patients to hospital personnel.

If attending or hospital personnel are examined or checked for evidence of tuberculosis, what methods are used?

	YES	NO
Questioned as to history of contact	20	
Physical examination	20	
X-ray	20	
Tuberculin test	14	6
Sputum examination	14	

As can be seen many hospitals did not fill out completely this part of the questionnaire. Unfortunately, it was not asked whether tuberculin tests or roentgenograms of the chest were made routinely as a part of the examination for tuberculosis. In 6 instances it was stated that tuberculin testing was not used but that roentgenograms of the chest were made, while in 3 hospitals tuberculin tests were done and roentgenograms of the chest made if indicated. Eight hospitals answered yes to making both tuberculin tests and roentgenograms, and 3 to both only when indicated. In the other positive answers to the questions, it seems that the procedures were done only when indicated.

If attending or hospital personnel are examined or checked for syphilis, what methods are used?

	YES	NO	NO DATA GIVEN
Physical examination	13		13
Blood examination	19	3	4

If attending or hospital personnel are examined or checked for gonorrhea infection, what methods are used?

	YES	NO DATA GIVEN
History of infection	12	14
Physical examination	12	14

	YES	NO	IF YES, HOW OFTEN			NO DATA GIVEN
			WHEN INDICATED	YEARLY	ONCE	
Vaginal smears	10	3	4	1	4	13

Are food handlers, maids, and kitchen employees checked for evidence of typhoid, dysentery infection, or carrier?

	YES	NO	NO DATA GIVEN
Physical examination	14	6	6
Stool examinations	13	8	5

Do you have a regular health service for your personnel?

YES	NO
14	10

Who examines your personnel?

Pediatrician	3
Doctor of internal medicine	11
General practitioner	4
Resident pediatrician and specialist when necessary	6

SUMMARY

From the accumulated data it would seem that there is no uniformity in the policy pertaining to the examination of hospital personnel for such transmissible diseases as tuberculosis, syphilis, gonorrhea, typhoid, and dysentery.

Examination of the medical staff is rarely performed except that 37 per cent of the hospitals require examination for tuberculosis of the intern and resident staff.

Tuberculosis is the only disease that appears to be considered a hazard either to the patient or to the personnel as 75 per cent of the hospitals do examine for this disease although only when indicated by some.

There is very little difference in the frequency of examination for tuberculosis and syphilis of the nonmedical personnel in contact with patients and food handlers. The latter, though, are examined oftener for gonorrhea, typhoid, and dysentery.

None of the hospitals reported transmission of any of the diseases from personnel to patient although one hospital reported "one suspicious incident of transmission" without naming the disease. Two hospitals reported transmission of syphilis and tuberculosis from patient to personnel.

Although no cases of transmission from personnel to patient were reported, it must be recognized that these diseases are transmissible and that they may be present with few if any symptoms in members of the personnel. It is possible then that their presence would not be recognized except by specific examination.

COMMENT

Our information indicates that many of the hospitals do not require an efficient check on the health of the entire personnel and that some hospitals are exceedingly neglectful in this respect.

We suggest that the children's hospitals of this country and Canada might greatly assist the work of the Committee on Contact Infections if they would require thorough, periodic physical examinations of all workers who come in contact with the patients, whether this contact is direct or indirect, as in the case of food handlers.

COMMITTEE ON HOSPITALS AND DISPENSARIES

Chairman, George F. Munns
Secretary, John A. Bigler
Murray H. Bass
Laurence R. DeBuys
Clifford G. Grulee
Lewis Webb Hill

Academy News

Region III will hold its annual meeting on May 16, 17, and 18, 1940, at the Muehlebach Hotel in Kansas City, Mo.

Region IV will have its annual meeting on May 30 and 31, 1940, in Seattle, Wash.

News and Notes

The **Society for Pediatric Research** will hold its annual meeting May 1 and 2, 1940, at Skytop Lodge, Skytop, Pa.

The **American Pediatric Society** will hold its fifty-second annual meeting on May 2, 3, and 4, 1940, at Skytop Lodge, Skytop, Pa. This meeting will immediately follow the meeting of the Society for Pediatric Research.

Announcement has been made of the bequest of $250,000 made by Dr. DeWitt H. Sherman to the University of Buffalo Medical School for the erection of a new medical school building. The bequest stated further that, if the new medical school building were erected during the life of Mrs. Sherman, this trust fund should then be used for pediatric education and research.

Following this announcement, Mrs. Sherman contributed an additional fund of $250,000, which will be used also for the erection of the new medical school building. These funds do not become available until the death of Mrs. Sherman. Dr. Sherman died February 1, 1940. He had been Professor of Pediatrics for many years at the University of Buffalo Medical School.